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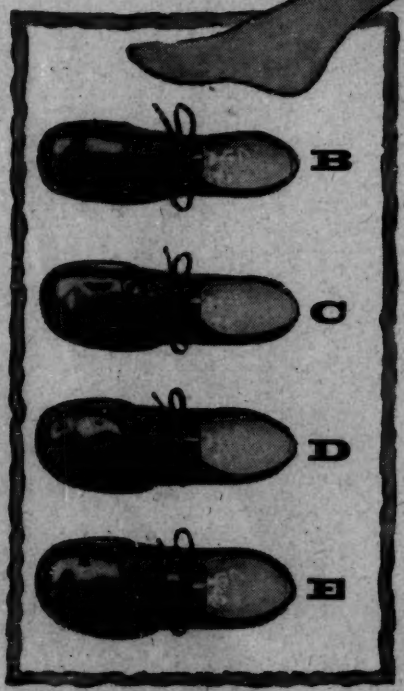

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY APRIL 1 1961

ACCIDENT NEUROSIS*

BY

HENRY MILLER, M.D., F.R.C.P., D.P.M.

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LECTURE I

At a time when fever hospitals are being closed and accident hospitals planned or opened, the fact that several recent lectures in this series have been devoted to various aspects of accidental trauma would not have disconcerted Dr. Gavin Milroy. His "suggestions" to lecturers of 80 years ago reveal an urgent preoccupation with what was topical in State medicine, and he could not but be impressed to-day that two short decades have witnessed the virtual displacement of the contagious fevers by trauma as a major epidemic scourge of our civilization. Each year more than a million people in Great Britain are injured at work or on the roads. Figures of such magnitude pose major problems of organization to the Health Service, but the functional nervous disorders which sometimes follow accidents have an additional importance to State medicine, since it has been widely argued that their very occurrence is in some way related to the machinery that society has evolved to deal with them.

The literature of accident neurosis is scanty, and it has received little attention from formal psychiatrists. Most papers on the subject are in the nature of occasional contributions, often more conspicuous as expressions of opinion than for their factual content. Indeed, the subject is so fraught with prejudice that it demands a conscious effort to maintain a clear distinction between fact and interpretation. This I will endeavour to do, and my material will fall into two parts—first, the presentation of clinical data derived from personal experience, and, secondly, a discussion of its possible medical and social significance.

The question of terminology is a vexed one, and the inelegant prefix of the title has been adopted reluctantly but advisedly. The term "traumatic neurosis" was coined by Oppenheim (1889), who attributed the condition to neuronal damage of a molecular nature. Whatever validity such a concept may have to the problem of cerebral concussion, it is clearly irrelevant in the present context: accident neurosis may arise quite independently of physical injury of any kind. Furthermore, the subsequent extension of Oppenheim's term to cover the results of so-called "psychic trauma" as well as physical injury has so far deprived it of any clear meaning that it is best discarded. The terms "compensation neurosis" or "litigation neurosis" have the virtue that litigation is a more constant feature of these cases than physical injury, but they prejudge the issue of aetiology.

*From the Milroy Lectures for 1961, delivered before the Royal College of Physicians of London on February 7 and 9.

The evidence presented here is based on personal experience of about 4,000 patients examined for medico-legal assessment after accidents during a dozen years of consultant practice. It includes an analysis of 200 cases of head injury recently examined for this purpose, and a follow-up study of 50 patients in whom gross neurotic symptoms after an accident had been found on examination more than three years previously.

Neurosis and Head Injury

The material under review in this connexion comprises 200 consecutive cases (152 male and 48 female) of head injury first referred for medico-legal examination between 1955 and 1957. The ages of these patients ranged from 2 to 84 years: 90%, however, were between 20 and 60, the average age being 42. All social strata were represented, from unskilled labourers to the peerage. The average interval between injury and first examination was 14 months. Ninety-four injuries were sustained in road and 106 in industrial accidents. The "industrial" group included a few patients injured in the course of non-industrial occupations. Of these 200 cases, 47 had gross and unequivocally psychoneurotic complaints.

In 22 other cases a post-concussional or post-contusional syndrome was complicated by psychoneurotic features. In nine further patients a true depressive syndrome of "endogenous" pattern succeeded the injury; and in one instance traumatic delirium following severe brain injury merged imperceptibly into a schizophrenic illness, in a man whose elder brother was already an established schizophrenic. In 34 other cases organic impairment of personality or intellect was encountered: all except three of these patients had suffered prolonged unconsciousness extending over periods varying from several days to many months. The three exceptions comprised an arteriopath of 66 in whom gross dementia followed a closed head injury characterized by only 15 minutes' unconsciousness; and two cases in which severe fractures of the skull had been unassociated with any impairment of consciousness.

Differential Incidence of Neurosis

Our main concern here is with the 47 cases with indubitably psychoneurotic complaints. Such a development was twice as common after industrial (33%) as after road accidents (16%). It was more than twice as common in men (27%) as in women (12.5%). This difference might at first sight be regarded as partly related to the preponderance of road accidents amongst the female cases. It is true that only six of these

resulted from occupational injuries, among which were two cases of gross psychoneurosis. On the other hand, 42 traffic accidents in women yielded only four instances of neurosis, whereas 12 were encountered amongst the 52 men similarly involved.

It is a widespread clinical impression that accident neurosis is commoner in older subjects, but no evidence is forthcoming from this material which favours the view that age is of much importance in relation to the syndrome—except that it was not encountered in childhood. Almost exactly half of these patients were over 40. Among these the incidence of neurosis was 24%, as against 21% in the younger group.

Relationship to Severity of Injury

In whatever way the cases are broken down they demonstrate an inverse relationship of accident neurosis to the severity of the injury. Gross psychoneurosis occurred, for example, in 31% of patients without radiological evidence of skull fracture, in 9% of patients with simple fracture, and in only 2 out of 25 patients who suffered compound fractures of the skull. In one of these a gross hysterical reaction complicated organic deterioration of personality and intellect following a severe brain injury, and the other patient was already a lifelong hypochondriac. A similarly inverse relationship is shown between the incidence of gross psychoneurosis and the duration of unconsciousness. The incidence of psychoneurosis in patients who were never unconscious was 42%. Amongst all unconscious patients the incidence was 14%. Where the post-traumatic amnesia (P.T.A.) was less than 15 minutes the incidence was 37%, and where it was more than this it was 10%. Of 48 patients with P.T.A. of more than 72 hours, only three showed residual psychoneurosis. One was a mental defective, one the lifelong hypochondriac already mentioned, and one a patient with a long history of recurrent psychiatric disability before his accident.

Predisposing Factors

The incidence of accident neurosis is related to social status. In the industrial group most of those who developed gross neurotic sequelae were unskilled or semi-skilled workers. Cases from this social group showed an incidence of neurosis of twice the average (47%). Amongst men, labourers, datal mineworkers, and the like furnished the bulk of cases. Amongst women, factory and office cleaners were conspicuous. More than half of the patients with accident neurosis came from the Registrar-General's social classes IV and V (semi-skilled and unskilled workers), as against a 38% representation of these social classes in the 200 cases reviewed, and 34% in the population of Northumberland and Durham as a whole. Among patients above the level of under-foreman or charge-hand, neurotic symptoms or prolonged incapacity subsequent to industrial head injury occurred in only 18% of cases.

The factor of social differential may also be related to the lower incidence of neurosis after road accidents, which cover a wider social range than the industrial group. Even here, however, a disproportionate number of cases occurred in those of lower social status, and the condition was distinctly rare among the professional or managerial patients examined. However, amongst the latter, one intelligent businessman and one professional man frankly admitted to making the most of their symptoms in the hope of turning minor injury to financial advantage.

It has often been suggested that the nature of the accident is a material factor in influencing the subsequent development of neurosis. Some of the accidents in which the patients under discussion were involved were of the most alarming nature, but out of 17 such outstanding instances neurosis developed in only two, and indeed many of the most disabling functional sequelae followed trivial blows to the head sustained during the course of some routine occupation quite devoid of special danger. However, the nature of the employment is possibly of some importance. The condition appeared to be more frequent in the employees of large industrial organizations or nationalized industries than in those working in the more intimate *milieu* of small businesses or on farms. The series is not a large one, and allowance must be made for local factors. However, it would appear that underground mineworkers and steel erectors, especially in the labouring grades, furnished a higher-than-average proportion of cases: such work is of course dangerous, and widely known to be dangerous, while claims for compensation are an everyday matter in the industries concerned.

In relation to personal predisposition, it has been stressed in psychiatric circles that accident neurosis tends to occur especially in patients with a particular type of personality—dependent, insecure, craving sympathy, and at the same time exhibiting well-marked paranoid tendencies. This may be the case, and such features are indeed often conspicuous by the time the patient is seen with the developed syndrome. However, in view of the absence of any valid parameter of personality, and of the fact that assessment of the patient prior to his accident is both subjective and retrospective, it can hardly be regarded as more than a clinical impression. Indeed, in response to direct questions few of these patients are prepared to admit to anything other than robust physical and mental health until the very day of the accident, while the collateral evidence of relatives and friends—so valuable in other psychiatric contexts—is often equally unreliable. Assessment of pre-accident personality therefore presents special difficulties, and depends to a greater degree than is usual on information from uncommitted sources such as the family doctor, and on the objective evidence of work and sickness records. Quotation of these often jogs the patient's memory for important events which—whether consciously or unwittingly—he had omitted from the most painstakingly elicited history.

With these qualifications, evidence of some significant predisposing factor or factors was found in 20 of these 47 cases in which gross neurosis had followed head injury. Because of the frequent tendency of these patients to conceal positive evidence in their pre-accident histories this figure is more likely to be an underestimate than an overestimate. However, the development of a major psychoneurosis of disabling severity in adult life (barring either a background of organic brain disease or camouflaged psychosis, or else a truly catastrophic emotional situation) usually implies a degree of predisposition hard to disguise even in the most cursory psychiatric history. The absence of any evidence whatever of predisposition to neurosis in more than half of these psychiatrically disabled patients is therefore a very striking feature.

Amongst the predisposing factors encountered in certain cases was below-average intelligence. In these

cases, however, emotional stability was more significant: several stable dullards showed no neurotic developments after their head injuries. A past history of evident emotional instability, invalidism, hypochondriasis, or prolonged incapacity after previous minor injuries was an unfavourable feature, as was a shiftless work record. Concurrent menopausal nervous symptoms, coincident hypertension, and arteriosclerosis were occasional factors. Responsibility for the patient's prolonged absence from work was often laid firmly at the door of the doctor—"he won't let me go back"—but in fact convincing evidence of primary iatrogenesis was rare.

Occupational Disability

The average duration of absence from work in 31 patients with neurosis who had returned to their employment when they were seen was six months. This figure must be considered in relation to the severity of the head injuries involved. Only 4 of these 31 patients had sustained fractures of the skull. Sixteen never lost consciousness, and in nine further cases the P.T.A. was measured in minutes; only six patients had been unconscious for an hour or more. This compares with an average period of four months' loss of work in 58 patients who had sustained simple fractures of the skull uncomplicated by neurosis. Forty-six of these patients had been unconscious, 23 for more than five days and only nine for less than an hour.

The average of six months' occupational disability with neurosis may be compared also with that in patients who had sustained compound fractures of the skull. Of 22 such cases, five were permanently disabled by epilepsy, hemiplegia, or organic mental change; and two others were away from work for two and a half and four years respectively on this last account. In the remaining 15 cases, however, the average period of absence from work after compound fracture of the skull was a little less than 4.5 months. These encouraging figures for early return to work after severe head injury are very similar to those given by Ritchie Russell (1934) in a survey of consecutive cases drawn from hospital practice. He also convincingly demonstrated the effect of the compensation issue in prolonging incapacity. The present figures demonstrate that, even where this factor is uniformly operative, all but the most severe head injuries cause less occupational disablement than accident neurosis.

Post-concussional Syndrome

In 36 of the 47 cases of gross neurosis described above the symptomatology was that of uncomplicated emotional illness, in which symptoms of organic pattern were entirely lacking. In the remaining 11 cases the actual disability at the time of the examination was predominantly and unequivocally neurotic in nature, but persisting post-concussional symptoms were also present. The consistency of the post-concussional syndrome of headache, postural dizziness, irritability, failure of concentration, and intolerance of noise argues a structural or at the least a pathophysiological basis. However, such symptoms are by no means invariable, even after material closed head injury, and in most uncomplicated cases the subjective disability is not of long duration. Unless the injury has been of some severity it is uncommon for a patient to be away from work for more than a few weeks after concussion sustained in sporting or other neutral circumstances.

In addition to the 11 cases in which gross neurosis complicated post-concussional symptoms, a post-concussional or post-contusional syndrome was also encountered in 73 other cases of closed head injury in the series, and also in 9 of the 22 patients who had suffered compound fractures of the skull. In none of the nine cases of compound fracture was it complicated by neurosis, but in 22 of the 73 other cases there was an admixture of emotional symptoms, such as sleeplessness, self-pity, depression, or frank anxiety, which were interpreted as indicating a neurotic superstructure. This view was usually also supported by the prolonged duration of the syndrome, its failure to improve, and the frequent claims of deterioration in a symptomatology which we know ordinarily tends to spontaneous improvement, and in which there is every logical reason to expect such a development.

Again, analysis reveals in these cases an inverse relationship between the severity of the injury and the development of neurotic symptoms. Of 49 patients in this series whose post-concussional syndromes followed head injuries associated with unconsciousness of more than five minutes' duration, only three developed persistent neurotic complications, while these were encountered in no fewer than 19 of the 24 patients in whom post-concussional symptoms of similar "physical" pattern followed head injury without loss of consciousness. In the post-concussional group also, neurotic complications were more than three times as common in the absence of skull fracture as in its presence.

These figures indicate that in this series persistence and psychoneurotic elaboration of the post-concussional syndrome bore an inverse relation to the severity of brain injury similar to that observed in the case of frank neurosis. They suggest that in this context at any rate the psychoneurotic component was an expression of whatever situational factors are responsible for accident neurosis in general, and not a function of structural damage.

In other ways also these 22 patients with psychoneurotically complicated post-concussional syndromes were comparable with the 47 examples of neurosis previously presented. By comparison with the 51 instances in which a post-concussional syndrome was uncomplicated by neurosis there was no difference in age incidence (the averages being 42 and 41.5 respectively) and evidence of neurotic predisposition was again found in less than half. Once more also, the neurotic complications showed a higher incidence in the lower social groups.

Depressive Illness Following Head Injury

The nine patients in whom depressive illness followed head injury stand out from the neurotic cases in many ways. In eight the depression was of classical endogenous type and in only one instance did real diagnostic difficulty arise. Seven depressive patients were over 40, the average age being 51. The head injuries were material in all but one instance: one patient had a fractured skull and six had been unconscious. Four patients had a previous history of depressive illness, and three others showed significant predisposing factors in the form of severe hypertension and arteriosclerosis, antecedent menopausal symptoms, and a long history of obsessional neurosis respectively. Two patients were suicidal. Five had been or were subsequently treated with electric convulsion therapy. In each instance improvement followed, even though the compensation issue remained unresolved. These were in fact the only patients in the whole series who exhibited a favourable response of psychiatric symptoms to treatment.

Clinical Features of Accident Neurosis

This syndrome is one of the most stereotyped in medicine. Sometimes the fright of the accident merges imperceptibly into a continuing complaint of nervous symptoms with an anxiety-depressive cast. More often, and especially where the symptoms have a frankly hysterical flavour, the condition develops after a latent period of weeks or even months. The general symptoms are remarkably constant, and amount to head pains (usually described as "terrible," "terrific," or "agonizing"), exertional or postural dizziness, irritability, failure of concentration, and restlessness. Sleeplessness is volunteered in rather less than half, but in reply to leading questions the patient will usually claim insomnia of psychoneurotic pattern (difficulty in getting off to sleep), restless sleep, and often nightmares related to his accident. Where there has been physical injury, complaints of intractable pain or other disability in the injured part are common, and these may be associated with motor weakness easily improved on persuasion, or anatomically incongruous sensory loss.

Objective signs of anxiety such as tachycardia, tremor, and axillary hyperhidrosis are, however, relatively uncommon, and have been found in less than 15% of personal cases. Gross dramatization of symptoms was recorded in more than half. On examination this may be evident in the way the patient shies away from the ophthalmoscope; by the groaning and quivering which ensues when forward spinal flexion is tested; by a flaccid grip easily strengthened by distraction or encouragement; or by the patient's slumping forward with head in hands during the consultation, requesting a glass of water. I had long regarded this last as a pathognomonic sign of accident neurosis, but I understand that it is often seen in women requesting termination of pregnancy on psychiatric grounds.

The behaviour of the patient with accident neurosis at the consultation is characteristic. If he is being examined at the request of the insurance company he frequently arrives late. He is invariably accompanied, often by a member of his family, who does not wait to be invited into the consulting-room, but who resolutely enters with him, and more often than not takes an active part in the consultation, speaking for him, prompting him, and reminding him of symptoms that may for the moment have slipped his memory. The patient's attitude is one of martyred gloom, but he is also very much on the defensive, and exudes hostility, especially at any suggestion that his condition may be improving. It is almost impossible to conjure up a smile to relax his appearance of preoccupied tension. His complaint of amnesia is often at variance with the circumstantial detail which invests his account of the events that led up to the accident many months ago. At some stage he will often insist that the cause of this was absolutely outside his control and that it was entirely due to someelse's fault. The "someone else" is rarely specified, but is usually "they"—in some vague way identified with the employing organization—or the unknown other motorist.

The most consistent clinical feature is the subject's unshakable conviction of unfitness for work, a conviction quite unrelated to overt disability even if his symptomatology is accepted at its face value. At a later stage the patient will declare his fitness for light work, which is often not available. The logic of prescribing light duties rather than his customary employment for the rehabilitation of the neurotic worker may appear obscure, but the reason why such a recommendation is often made by the general practitioner and echoed in consultant reports is clear: light work is better than no work at all, and it is generally appreciated that unless the doctor goes half-way to meet him—and especially if he provokes actual hostility—the patient's complaints will be intensified and disability further prolonged. The equanimity with which these patients will accept the tedium of months or even years of idleness, apparently unmitigated by any pleasurable diversion, is remarkable.

Another cardinal feature is an absolute refusal to admit any degree of symptomatic improvement. With the exception of a few well-defined conditions such as traumatic arthritis and causalgia, there are no physical results of injury the discomforts of which do not in the course of time become somewhat less intense. Far from accepting the suggestion of such improvement, these patients often make the improbable claim that pain at the site of injury has steadily become more severe over a period of months or years.

Equally characteristic is the patient's attitude to medical attention and treatment. In industrial cases periodic attendance on the general practitioner is necessary in order to obtain successive certificates of unfitness for work, but in other instances it is remarkable that the patient will complain bitterly of disabling nervous symptoms lasting for many months—for which she has never once sought medical treatment. In a number of personal cases the aid of the general practitioner was invoked only after searching questions about such treatment had been asked during a consultation for medico-legal purposes.

The Case History

A case history synthesized from several hundred personally recorded would read somewhat as follows. An unskilled labourer, either with an uneventful previous history or who had perhaps suffered earlier accidents in which minor injury was followed by disproportionately long disablement, sustains a bruise when he trips over a piece of wood carelessly left on the factory floor. Although similar occurrences in his home have never been met with anything more than an expletive, he goes straight to the works ambulance-room, where a dressing is applied and the incident duly recorded in the accident book. The injury is trivial. He completes his shift and possibly puts in two or three further days' work. He discusses the incident with his friends, and consults a union official, who encourages him to formulate a claim "just in case the injury should give trouble at a later date." The union official cannot be blamed for such advice. Official posters exhort the workman to report even trivial accidents at once—and in any case a late claim is always suspect.

The man stays away from work to visit his doctor, who knows his job is heavy and acquiesces in his suggestion of a week's rest. During this week at home he develops headaches, sleeplessness, nervousness, and loss of appetite: he is irritable and easily startled.

It is easy to feel in retrospect that robust handling by the doctor at this stage might have got the man back to work. Sometimes this is true: everyone knows that for one reason or another some doctors abet scroungers, and there are many more who acquiesce in the lay conception that absence from work is in itself a form of

medical treatment. But in this connexion the difficulties should not be minimized: there is often another doctor around the corner who may be more compliant.

At any rate, a process has now been initiated which may lead to months or even years of disablement. Some of this time is spent—unfortunately with tacit professional support—in pointless attendance at the physiotherapy department of a local hospital, where his now normal limb is rubbed, heated, and exposed to coloured lights. Such occupation alternates with aimless wandering about the streets, watching television, and sitting moodily in the house. It is punctuated by lengthy periods in an industrial convalescent home in the country—a residential club where he can compare notes with a handful of fellow sufferers.

Throughout this whole period he sees little of his own doctor and a good deal of solicitors, union officials, and medical consultants to whom he is referred for assessment. From his practitioner he merely accepts certificates of unfitness for work; there is by now a tacit understanding between them that no kind of treatment will influence his symptoms at the present juncture. This view is likely to be confirmed by any psychiatrist to whom the patient is referred, and if the doctor does in fact make some well-intentioned attempt to help him by prescribing a sedative or ataractic the patient will tell subsequent inquirers that these were quite useless, and that he has had "no treatment, only some tablets." With repeated examinations and interrogations the familiar syndrome gradually assumes its usual florid form. The case involves an allegation of negligence under common law, and is ultimately put down for hearing at the next assize court; but because the civil list is too full—mainly of similar proceedings—or for some other reason, it is adjourned, and ultimately comes to trial months later and several years after the accident. In the interim it is clearly against the man's financial interest to return to any kind of work, or to admit the faintest improvement, while a claim of deterioration can react only to his pecuniary benefit.

Finally the case comes to trial. Even at this stage eleventh-hour settlement after hard bargaining is the likeliest outcome. Once in court the issue of negligence may be unproven and the case may collapse, leaving the man without even the solace of financial benefit. More often, however, it is easy to prove a technical breach of a minor regulation, and an award of some kind is made—perhaps a few hundred or even sometimes a few thousand pounds. In the course of the case the counsel for the employer or the insurance company expresses confidence that once it is settled rapid improvement will occur. Counsel for the man enters the caveat that this is not invariable, and that many such patients suffer persisting disablement long after settlement, and sometimes permanently. Neither they nor their expert witnesses, nor the judge who must assess damages, can give a reliable prognosis or even a valid assessment of statistical probabilities.

It is remarkable that in a country where industrial accidents cause 800,000 new insurance claims and the loss of 16,000,000 working days annually, where there are more than 250,000 road injuries in a similar period, and where three-quarters of all accidental injuries occur under conditions where compensation is potentially payable, no proper inquiry has ever been conducted into the fate of patients with this well-defined syndrome after they leave court. The barrister's interest ceases the moment judgment is given. The insurance company is licking its wounds and wondering whether it might not have been cheaper to settle—or not to settle. The medical witnesses' interest, already vitiated by the unpredictable dislocation of a busy professional schedule, has evaporated. The only person in a position to know what happens next is the general practitioner—and his part in the case has so far been negligible.

Prognosis of Accident Neurosis

There are several indications that the prognosis of this condition is more favourable than the apparent severity of symptoms at the time of settlement would suggest. The first is that, amongst a number of patients personally seen in this or some other connexion who had previously suffered from and been compensated for a similar condition, not one has ever admitted to any psychiatric disability remaining from the first accident. The second is that, although the syndrome is a very common one in an industrial area, patients with this disorder in whom the legal issue has been resolved are conspicuously rare amongst the thousands who seek treatment for functional nervous disorders. Thirdly, it is significant that of the many ex-Service men who were drawing pensions for the rather similar condition of war neurosis at the end of the second world war, in the vast majority of cases symptoms cleared up within a few years of demobilization. In my experience of these ex-Service cases symptoms persisted only in those heavily predisposed to neurosis; in patients with very inadequate personalities; and in a very small group of patients, apparently previously normal, who had been subjected to prolonged and overwhelming stress, not infrequently occurring in situations which evoked feelings of guilt about the fate of their comrades. Even where psychoneurotic symptoms persisted or persist to the present day, material disablement from the occupational point of view is extremely rare.

The literature of accident neurosis has been reviewed by Pokorny and Moore (1953), but it contains little reliable information on the question of prognosis. Discussion by Purves-Stewart (Buzzard *et al.*, 1928) and by Smith and Solomon (1943) supports the view that it is essentially favourable. Purves-Stewart reported a small group of personal cases, all but one of which promptly recovered and returned to work on settlement. He made two points which are supported by personal experience. These patients are difficult to trace, and the large majority withdraw themselves completely from any form of medical supervision once the case is settled. Secondly, early and complete recovery is as likely to follow the irrevocable rejection as the success of the claim for compensation.

The paucity of reliable figures in this connexion stimulated me to follow up 50 consecutive cases of accident neurosis personally examined between three and four years ago.

Follow-up Study of 50 Cases of Accident Neurosis After Settlement

At the time of the first examination and at the time of settlement of their claims for compensation, each of these 50 patients (41 men and 9 women) complained of disabling nervous symptoms occurring after accidents. In 31 the accident had been industrial, in 18 a traffic accident. The ages of the patients ranged from 22 to 70, the average being 42.

Twenty-four of these patients were labourers or unskilled or semi-skilled workers falling into the Registrar-General's social classes IV and V—a proportion again much higher than that found in the population at risk. Fifteen were skilled workmen, three were (untrained) nurses. Other occupations represented were housewife, clerk, shop assistant, university student, haulage contractor, building contractor, and company director.

In three cases there had been no physical injury whatever, while in 35 it had been trivial—head injury without impairment of consciousness (13 cases) or with only momentary concussion (4), general shaking and bruising (10), minor back injury (4), lacerations of face and arm, and bruising of hand; in two further cases a finger was fractured. In the remaining 12 patients injuries were more severe—major fractures, multiple general injuries, or head injury with prolonged unconsciousness (30 minutes to four days).

In 36 of the 50 cases the psychiatric picture was typical of "accident neurosis," with conspicuous depression, restless sleep, hypochondriacal invalidism, disgruntlement, and self-pity in varying proportions. In 21 of these 36 cases there were positive physical or psychiatric signs of a hysterical reaction. In another five, phobic symptoms were related to the circumstances of the accident or to the occupation generally.

In four other cases a post-concussional syndrome after trivial head injury was elaborated and prolonged for more than two years, with positive evidence of hysteria. In four patients constant intractable disabling pain at the site of injury was the main symptom. In all three patients with hand injuries (two with fractured fingers, one merely bruised) a similar complaint was complicated by hysterical contracture of one or more fingers. There were two patients in whom depressive and psychoneurotic features were inextricably mixed, and one unusual instance in which a patient subjected to a particularly terrifying experience developed an anxiety state of great severity which rapidly responded to psychiatric treatment—after which he abandoned his claim for compensation.

Personal predisposition to neurosis was evident in the previous histories of only 15 of these 50 cases. Six of the predisposed patients were chronic neurotics, well known to their general practitioners over many years. One was a previous subject of depressive illness. In three other patients the history revealed earlier episodes of neurotic response to stress—for example, invaliding from the Army with intractable headaches which cleared up after discharge. Of the remaining five, four were inadequate or immature personalities with shiftless work records (one being an alcoholic) and one was a dullard.

Of these 50 cases, 42 had been settled by negotiation out of court, and in four the claims had been withdrawn or abandoned. The four remaining cases all came to trial, and in each instance the claim for compensation was rejected. In two instances the complainant failed to prove liability. In one the judge gave it as his opinion that the patient was malingering, and in the other that his chronic neurotic symptoms were not due to the accident. The average delay between accident and settlement was 26 months. Damages negotiated ranged from £20 to nearly £5,000, and averaged £454. In some instances, however, this represented an assessment based on the sum of physical and psychiatric disabilities, and in a few it was made on the basis of only partial liability. In a group of cases where physical injury was trivial and residual disability unequivocally psychiatric the average award was only £152 (£181 in men, £83 in women).

The average interval between settlement and re-examination was a little over two years. Only two of the patients had undergone psychiatric treatment for their nervous symptoms (Cases 34 and 36, see below). All but four of the 45 previously employed had returned to their own or similar work. One of the four was in hospital undergoing plastic surgical treatment for his severe general injuries. One was a married woman who had not resumed her part-time occupation because of domestic commitments.

Illustrative Cases

Two of the 50 patients were occupationally disabled by psychiatric symptoms at the time of re-examination.

Case 30.—In 1955 a 42-year-old unskilled colliery labourer sustained a minor head injury without loss of consciousness. He was a man of low intelligence with a history of much vague ill-health in the past. After this head injury he worked for a week without interruption, but a few weeks later he developed attacks of weakness of the left side of the body and clouding of consciousness. When seen at this time he presented a difficult diagnostic problem, but exhaustive in-patient investigation was entirely negative, and attacks observed while he was in the ward were grossly hysterical. Apart from these attacks he had no disability whatever. The case was settled out of court by negotiation and he was awarded more than £4,000 in damages. It would appear that a diagnosis of traumatic epilepsy was sustained in this negotiation and subsequently accepted by the Ministry of National Insurance, which continued to pay him a pension of £3 16s. 6d. weekly. Since this time he has never returned to work. Re-examination in 1960 again failed to confirm epilepsy and yielded positive evidence of hysteria.

Case 34.—In 1954 a 27-year-old labourer sustained a minor concussion and bruising of his back when he was knocked off his bicycle. Repeated clinical and radiological examinations were negative, but he continued to complain bitterly of pain in the back and down the legs. There was nothing in his past or family history to indicate any predisposition to neurosis, but he continued to complain and did not return to work. He had a great deal of out-patient physiotherapy and rehabilitation and numerous conflicting specialist opinions. When examined two years after the accident there were no abnormal physical signs except those of gross hysteria. The case was settled three years after the accident for more than £2,500. However, his hysterical gait continued for 18 months after settlement, finally responding to suggestive psychotherapy in a psychiatric unit. Two years after the accident there was little or no real disability except that he continued to use a stick unnecessarily. He had never returned to work and shows no signs of doing so. He continues to draw a National Insurance pension for industrial injury.

Both these disabled patients were under regular medical treatment from their general practitioners. Of the remaining 48 patients, only five were in receipt of any form of medical treatment. The first of these was the severely injured man previously mentioned, whose marked hypochrondrial-depressive reaction had cleared up rapidly after a substantial financial settlement for his injuries. The second (heavily predisposed) patient, whose psychoneurotically patterned sequelae of minor head injury gave no trouble for two years after he had been compensated to the tune of £400, was suffering from a recurrence of anxiety symptoms in relation to the stress of several months' unemployment because of

redundancy. In three others psychoneurotic symptoms had persisted since the accident but were not causing occupational disability.

Case 13.—A 26-year-old labourer returned to work six weeks after a brief concussion sustained by striking his head on a beam at work, but although under no form of medical treatment he was so often late or absent that he was dismissed four months later. During the subsequent three months he held two light jobs for short periods. He then gave up work altogether, and 18 months after the accident he made a claim for several thousand pounds in damages, complaining of constant and steadily worsening headaches and dizziness. By the time the case was settled out of court (for £400) he had been idle for more than two years. After settlement he continued constantly to attend his doctor with headache, backache, insomnia, lassitude, etc., and to draw disablement benefit and hardship allowance under the National Insurance Acts. Finally a medical board terminated his pension, after which he promptly returned to work.

My original notes on this patient commented on his evasive manner and deplorable pre-accident work record, though he had insisted to several examiners on his "perfect health before the accident." His general practitioner's records, however, go back to a decade before his injury and reveal him throughout as "a regular attender at the surgery with a variety of complaints of the same kind as those he brought along after the injury . . . he has been the same ever since he left school."

Case 22.—While handling a piece of light furniture a 49-year-old shop assistant stated she "cricked her back." She did not report the injury, but sent for her doctor the next morning. She was confined to the house for 16 weeks, and, although there were at no time any positive clinical or radiological findings, she remained away from work for two years, during which period she attended the physiotherapy department of the local hospital. On examination at the end of this period she claimed total disablement by continual and steadily increasing pain in the back and down the left leg; and by depression, anxiety, and sleeplessness, which had begun 14 days after the accident. Total superficial sensory loss of stocking distribution up to the groin on the left side was the only abnormal physical finding: her behaviour was histrionic in the extreme. At this stage the case came to trial, and her claim for damages was dismissed on the grounds of lack of evidence that there had been an accident. She subsequently returned to light work, but continued to attend her doctor with multiple symptoms. He reported that "her condition is the same as it has been for 10 years. She was a neurotic before the accident, and I expect she will remain so."

Case 36.—A housewife aged 39 was treated by her doctor for functional nervous symptoms, and was given a prescription for a capsule of "carbrital" to be taken each night and for two codeine tablets to be taken three times a day. Unfortunately the labels were placed on the wrong boxes and the patient took two carbrital capsules on the same morning, with the result that she became drowsy. The error was discovered and caused disproportionate alarm. A pharmacist administered stimulants. The patient's general practitioner advised that she be kept awake, and sent her post-haste to hospital, where her stomach was washed out. Within the course of a few days she was in an extremely emotional state, though she had, of course, recovered completely from the "overdosage." Three months later she claimed gross and disabling psychiatric symptoms which she said had been greatly increased by the experience. Both she and her family attributed her condition entirely to the unfortunate accident and appeared almost to have forgotten her earlier history. The case was settled by a small payment a few months after it happened. Since then the patient has had a good deal of psychiatric treatment, including brief admission to two psychiatric units for electric convulsion therapy. Review of the case-records indicates that recurrent depressive episodes had begun several years before the incident of the tablets in 1956.

In summary, only 2 of these 50 unselected patients with accident neurosis were still disabled by their psychiatric symptoms on re-examination two years after settlement. Both instances were characterized by diagnostic confusion, substantial lump-sum payments, and continuing National Insurance pensions for the results of the accident. In three other cases psychiatric symptoms persisted without occupational disablement: in each instance similar symptoms had been present for many years before the accident. Symptomatic recovery in the remaining 45 patients was as complete as their subsequent medical and occupational records indicated. The most they could muster were a few trivial residual symptoms of which "a queer feeling as I turn on the vacuum cleaner" and "some nervousness on overtaking in traffic" are fair examples. Of special interest was the disappearance of contractures in three cases of hand injury: two of these patients claimed some local discomfort in cold weather. Occupational phobias (for work at heights, driving heavy vehicles, and underground work) had also cleared up, and all five of these patients had returned to their previous employment.

Of 15 patients predisposed to neurosis, 11 had recovered after settlement; of 35 without predisposition all but one had recovered completely.

[Lecture II, with a bibliography, will be published in our next issue.]

LEPROSY: A REVIEW OF 79 PATIENTS SEEN IN LONDON

BY

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Leprosy became a notifiable disease in Great Britain in 1951. No figures have yet been published from official sources concerning the number of notified cases in this country in 1960, but Cochrane (1960) stated that the number of notified cases in England and Wales was 267. Eight years earlier he (Cochrane, 1952) quoted the figure of 100 notified cases in the same area. This increase in the incidence of the disease is to be expected in view of the post-war influx of persons from endemic areas.

The number of cases present but not notified must vary in different countries. Cochrane (1952), referring to 100 cases then notified in England, thought that there were perhaps 50 further cases undiagnosed or not yet reported, while Canizares and Combes (1952), reporting 32 cases of leprosy in New York State, concluded that most leprologists agree that for each reported patient there are at least three unreported or undiagnosed.

In the present series of 79 cases, two-thirds of the patients were immigrants from the Commonwealth who had arrived in Great Britain during the past decade. Although the incidence of leprosy is low in Great Britain, diagnosis often presents difficulties to doctors in this country, and for this reason the present series of cases is reported.

Of the 79 patients with leprosy registered at St. John's Hospital for Diseases of the Skin, London, all but seven had returned to Great Britain or immigrated since the second world war; 28 were referred to the hospital by general practitioners; and the remainder were referred by consultants for further investigation and were seen by the Adviser in Leprosy to the Ministry of Health or were already under his supervision.

Country of Origin

Eight patients born in Great Britain and one in central Europe acquired the disease while working in endemic areas. The largest number of immigrants (42) came from India. Of those, 5 were of European stock and 27 of mixed parentage, some of whom were European in appearance. This is of importance, as is discussed below, since leprosy in patients not racially pigmented may be more readily confused with dermatoses seen in this country. Only three patients were from Pakistan; the remainder were from Cyprus, West Africa, Burma, Ceylon, the West Indies, Malta, Aden, Hong Kong, and Malaya (Table I).

TABLE I.—*Country of Origin in 79 Patients with Leprosy*

Great Britain	8*	Pakistan	3
Austria	1*	Ceylon	3
India (Indian 10, Anglo-Indian 27, European stock 5)	42	West Indies	3
Cyprus	6	Malta	2
West Africa	4	Aden	1
Burma (all Anglo-Burmese)	4	Hong Kong	1
		Malaya	1

* Had worked overseas in endemic area.

Patients Diagnosed Before Arrival in Great Britain

Twenty-four patients (including two Europeans) were aware that they had been treated for leprosy before arrival in this country; 17 of these sought advice at once, all but one requiring treatment, and in eight of these, acid-fast bacilli were present in histological sections of the skin. These patients presented no public-health problem, since having sought advice, they were easily supervised. The remaining seven, however, believed that they were cured, and on relapse there was considerable delay before the disease was recognized; acid-fast bacilli were present in histological skin sections in five of these (Table II).

TABLE II.—*Presentation with Leprosy in 79 Patients*

Originally diagnosed in country of origin	24	Continued under supervision on arrival in Great Britain	17
		Presented as fresh cases in relapse	7
First diagnosed in Great Britain	55	Symptoms developed after arrival in Great Britain	31
		Symptoms present before arrival in Great Britain	22
		Date of onset of symptoms uncertain	2

It is doubtful whether compulsory declaration of previous treatment for leprosy by patients arriving at ports in this country would be an effective measure, since initially a number of patients have a fear, fortunately groundless, of enforced segregation and social ostracism. One patient from Malta sought treatment in this country to avoid enforced isolation, and I understand that this practice is not uncommon. The point is well illustrated by the following case history.

A married Cypriot woman aged 39 developed urticarial lesions and erythematous plaques on her skin while resident in this country. Her husband was confined in a leprosy colony in Cyprus. Her general practitioner found areas of anaesthesia and made the clinical diagnosis of leprosy. The patient, fearing segregation, refused to submit to further investigation. Later, when the risk of infecting her daughter was stressed, she agreed to allow her doctor to perform a biopsy in his surgery and the diagnosis was confirmed at a reference laboratory. Her daughter was subsequently found to be infected. Both patients then agreed to accept treatment, being assured that hospitalization was voluntary. Later, with some elementary precautions, treatment was continued under domiciliary supervision.

It may be stated at this point that leprosy is notifiable confidentially to the Chief Medical Officer at the Ministry of Health. This raises the question of the infectivity of cases so notified. Two main types of leprosy are recognized. Firstly, tuberculoid leprosy, in which the immunity response is high, skin lesions when present are well defined, and very few cases—that is, those that are in reaction and bacteriologically positive—are infectious. Secondly, lepromatous leprosy, in which the immunity response is low, and most cases—that is, those that are active and bacteriologically positive—are infectious. Some patients do not fall clearly into either of these categories; one such group, known as diamorphous (Cochrane, 1959) or borderline, is referred to in the present series of reported cases. This diamorphous (borderline) group consists often of relatively early cases, and the nature of the tissue response is not clearly evolved but may show predominantly lepromatous or tuberculoid features. Such cases are also infectious when in reaction and bacteriologically positive.

The total number of infectious patients seen in this country is small, and if their treatment presents difficulty in a general hospital they can be admitted to one of two institutions in England devoted entirely to their care. In nearly all cases the patients have agreed to be admitted on a voluntary basis when the necessity has arisen, and, failing this, have co-operated in taking such precautions as are necessary to prevent their being a danger to others if supervised at home. Many authors have stressed the high natural immunity of most adults to the disease and the necessity for skin-to-skin contact with a susceptible person, frequently a child, before infection can be transferred from an "infectious" case. Doull *et al.* (1945), in a study from the Philippine Islands, have shown that males are more susceptible to the disease than females. The high incidence in children might be explained partly on the basis of frequency of skin-to-skin contact.

Patients Diagnosed After Arrival in Great Britain

In 55 patients the diagnosis of leprosy was first made in this country (Table II). The long incubation or latent period of the disease is illustrated by the fact that in 31 cases symptoms began after arrival in this country; in 10 patients the interval between leaving the endemic area and the onset of symptoms was from three to eight years, and diagnosis was still further delayed. A case in point was that of the Cypriot, described by Haber (1944), who came to England in 1935, developed nodules on the forehead in 1939, and was diagnosed when under treatment for syphilis in 1941.

Of the patients first diagnosed in this country 22 had had symptoms for a period varying from 3 months to 21 years before arrival in England. It may be asked whether any of these cases were infectious at the time of entry. Three cases were potentially infectious: one was already under investigation, having been sent home from the armed Forces overseas; the second patient

had lepromatous leprosy but was diagnosed within six months of arrival. The third patient had neurological signs and symptoms only, which he attributed to an injury; his skin lesions were diagnosed soon after their onset, which occurred when he had been in this country for 18 months. The remaining 19 patients in this group had tuberculoid or dimorphous (borderline) skin lesions, many of them trivial, or had only neurological lesions.

Lastly, in two patients diagnosed in this country the date of onset of symptoms was uncertain.

Indigenous Leprosy

Newman (1895), referring to leprosy in the British Isles, concludes that "the endemic disease reached its zenith in the thirteenth century or earlier and declined till final extinction in the eighteenth." In the nineteenth century the Royal College of Physicians of London Report (1867) refers to a "few rare cases of indigenous origin," citing one case seen at the Edinburgh Infirmary and another at Guy's Hospital. These were presumably contact cases, as were three cases discussed in Dublin (Benson, 1877).

No further report appears until the present century, when Macleod (1925) refers to three contact cases; all were boys born in different parts of Great Britain who had not been abroad. No subsequent reports have been published, but in one contact case in the present series it is uncertain whether the infection was acquired before or after the family arrived in England.

A married woman aged 26, who had developed an early lesion of indeterminate nature at the age of 10 years when in India, did not seek advice until she had been in England for 18 months. She then had lepromatous leprosy. Her son, aged 3 years, was examined as a contact and found to have a tuberculoid lesion on the left cheek which had been present for four months. The mother accepted in-patient treatment and the child's lesion responded well to therapy.

The value of frequent examination of family contacts, especially children, is well illustrated by this case.

Clinical Manifestations

A detailed description of the clinical manifestations of leprosy is out of place in this context. Cochrane (1959) has emphasized that the two cardinal signs of leprosy are the presence of anaesthesia and the finding of *Mycobacterium leprae*. It is usually the case that lesions which are not anaesthetic contain acid-fast bacilli; if that is not so, then a thorough clinical examination will usually reveal thickening of the peripheral nerves and areas of anaesthesia over the limbs, in particular over the hands and the extremities of the lower limbs. Such criteria should be applied to any person in this country who has lived in an endemic area and presents with an unusual skin disease.

Some aspects of the clinical features of the present series of cases merit consideration.

Erythematous Skin Lesions.—Such lesions, whether nodules, macules, or infiltrated lesions, commonly occurred on the face. Further examination of the entire skin area, despite the patient's reluctance and denial of other lesions, often revealed further lesions, especially on the elbows, buttocks, or legs. Some lesions were reddish brown in colour and others were scaly. Five such patients were referred to hospital, the provisional diagnoses being dermatitis, eczema, epidermophytoses, seborrhoeic dermatitis, and ringworm.

Annular Lesions.—In the dimorphous (borderline) cases annular erythematous lesions are seen. One such patient was of especial interest.

A 39-year-old Spaniard of Jewish extraction arrived in England in 1947. Eight years later he developed erythematous macules starting on the face. For two years he was treated as a case of erythema annulare at another hospital. The diagnosis of leprosy was made in 1960. when he was referred by his family doctor to St. John's Hospital. The lesions were found to be anaesthetic.

Acute Erythema Nodosum or Urticaria-like Lesions.—Two patients presenting with erythematous macules resembling giant urticaria and areas of oedema illustrate the differential diagnosis from drug eruptions. One patient developed such an episode when under treatment with streptomycin for pulmonary tuberculosis, the other developed a widespread macular rash when a septic lesion was treated with penicillin; in neither case had leprosy been diagnosed before. The relationship of the eruptions to the drugs in these cases is uncertain, if not fortuitous. Muir (1938) associates the lepra reaction with debilitation due to illness or with drugs such as iodides, arsenicals, or mercurochrome.

Granulomatous Lesions.—In three cases the initial diagnosis was sarcoidosis. A similar diagnosis was considered in a 10-year-old boy but rejected in favour of lupus vulgaris, for which he was treated for three years. At about this time several cases of leprosy were seen, and this diagnosis was considered and proved correct. Two patients had a positive Wassermann reaction; one who gave a history of syphilis was reported by Haber (1944), who emphasized that a false-positive Wassermann reaction occurs in some types of leprosy.

Neurological Lesions.—21 patients had neurological symptoms or signs other than thickened nerves or symptomless areas of anaesthesia. Paraesthesiae or numbness had been noticed by eight patients, four of whom had had such symptoms for several years before skin lesions appeared, and in some cases paraesthesiae were related by the patient to an injury. Motor lesions were present in seven patients, two of whom had facial weakness. Seven patients had trophic ulcers on the feet and one had cigarette burns on the fingers. Three patients presented clinically with trophic ulcers.

A West African man aged 23 was treated at a casualty department for an indolent ulcer on his foot which had previously been injured by a nail. 16 months later he developed obvious cutaneous lesions and leprosy was diagnosed at another hospital.

A man aged 25, born in India, developed a boil on his calf which was painless but did not heal. Three months later his doctor referred him to a dermatologist when erythematous lesions appeared.

A man aged 57 presented with swelling and ulceration of the right foot. Examination revealed the characteristic picture of leprosy.

Finally, the importance of anaesthesia and of thickening of cutaneous nerves if seen in cases presenting with a patch of hypopigmentation cannot be over-stressed, for such hypopigmentation in dark-skinned patients can readily occur with inflammatory states such as tinea, healing impetigo, and eczema.

Summary and Conclusions

Seventy-nine patients with leprosy have been seen at a hospital for skin diseases in London. Two-thirds of these patients immigrated to Great Britain during the

past decade. The countries of origin of these patients, their manner of presentation, and some diagnostic difficulties are described.

At some time while these patients were under observation in this country, acid-fast bacilli were found in the skin of at least one-third, at which stage they were potentially infective; but fortunately the resistance of the adult population to the disease is high. Intimate contact is necessary before a susceptible person can acquire the disease, although such contact need only be brief. The public health aspect of this disease in some respects is similar, on an extremely limited scale, to that of pulmonary tuberculosis, in which only a proportion of the 345,000 cases at present on the chest-clinic registers in England and Wales are "open"—that is, potentially infective.

Although some cases are self-healing, others progress to more serious and permanent complications. An awareness that the disease exists and has increased in this country will lead to earlier diagnosis. The following quotation from the Royal College of Physicians Report (1867) is of historical interest and applies in some measure to the situation in the present century.

"A few rare cases of indigenous origin have been met with in the British Isles during the present century; but by far the majority of the examples of disease which have been recognized in this country have occurred in persons who either have been born in one of our tropical possessions, or have been resident there. Such instances appear to be less infrequent than is generally imagined; and it also seems not improbable that some anomalous forms of intractable skin disease may be vestiges or obscure manifestations of a partially leprous diathesis."

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REFERENCES

Benson, H. (1877). *Dublin J. med. Sci.*, **63**, 562.
Canizares, O., and Combes, F. C. (1952). *N.Y. St. J. Med.*, **52**, 2123.
Cochrane, R. G. (1952). *Publ. Hlth. (Lond.)*, **65**, 197.
—— (1959). *Leprosy in Theory and Practice*. Wright, Bristol.
—— (1960). *Med. Press*, **243**, 77.
Doull, J. A., Guinto, R. S., Rodriguez, J. N., and Bancroft, H. (1945). *Amer. J. trop. Med.*, **25**, 435.
Haber, H. (1944). *Lancet*, **1**, 629.
Macleod, J. M. H. (1925). *Brit. med. J.*, **1**, 107.
Muir, E. (1938). *Leprosy*, 6th ed. Indian Council, B.E.L.R.A., Delhi and Simla.
Newman, I. (1895). *Prize Essays on Leprosy*. New Sydenham Society, London.
Royal College of Physicians of London (1867). Report on Leprosy.

The All-India Institute of Medical Sciences has now received the donation of books and journals made to it by the late Professor J. F. Fulton from his personal collection. The Rockefeller Foundation financed the transport of the consignment, which included 451 books—mostly physiological and neurological works, a complete set of the *Journal of Neurophysiology*, and a number of volumes of other journals. A special bookplate was sent with the books, and when the library of the institute is completed it is hoped that a separate section will house the collection and be named after Professor Fulton.

STUDIES IN PORTAL HYPERTENSION

FACTORS AFFECTING OPERATION MORTALITY

BY

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The evaluation of shunt surgery for portal hypertension awaits a more definite appraisal of the natural history of the disease. One frequent criticism is that operation can be offered only to patients with good liver function who would survive for a long period of time without operative treatment. Should the mortality from the operation be high, a group of such patients might demonstrate a poorer survival time than a group treated conservatively. Nachlas (1958) suggests that the operative mortality may be greater than the risk of death from haemorrhage. He records an operative mortality of 18% among 440 cirrhotic patients collected from the literature between 1948 and 1956.

It is our belief that the operation is of value, but its application will be extremely limited unless the operative mortality is low. We report our series of 33 patients in whom a portacaval or splenorenal shunt operation was carried out. The operative mortality was zero. Comment is made on the factors that will keep the mortality at a low level. This series is a consecutive one and includes our total experience of the operation.

Clinical Findings.—As operative mortality may be defined in a variety of ways it is important at the outset to give our own definition. We believe that a patient who dies before leaving the hospital after an operation must be counted as an operative death. No patient in this series was discharged before his wound was soundly healed or before he was able to walk and was well enough to go to his own home.

The data relevant to the patients in this series are given in the Table. In all except one of the patients the indication for operation was haemorrhage from the varices which had required transfusion for its correction. In the one exception the indication was the size of the spleen. As this patient had portal hypertension it was decided to perform a splenorenal anastomosis.

Criteria of Operability.—In this we have been guided by some of the criteria laid down by Linton (1951), particularly the following: (1) the serum albumin should be greater than 3 g./100 ml.; (2) the serum bilirubin should be below 1 mg./100 ml.; and (3) ascites should be absent. As time has gone on and we have gained more experience with the operation, these criteria have been relaxed and no patient has been rejected for operation on account of any one of these factors alone. Patients with gross ascites are not accepted unless this can be substantially reduced by medical treatment. The preoperative levels for serum albumin and bilirubin in the patients in this series are given in the Table.

Factors Contributing to a Lowering of the Operative Mortality.—The operative techniques of portacaval and splenorenal anastomosis have been described elsewhere (Riddell and Cassie, 1959) and do not differ substantially from those in use at other centres. The causes of death

to be anticipated from these operations are liver-cell failure, ammonia intoxication, and the effects of haemorrhage. We believe that the following factors rather than the operative technique contribute to the safety of the operation. These are thorough preoperative preparation, the greatest attention and care in controlling haemorrhage during operation with immediate and

Details of Cases

Case No.	Sex and Age	Diagnosis	Preoperative Level		Ascites	Type of Shunt
			Serum Alb. (g./100 ml.)	Serum Bilirubin (mg./100 ml.)		
1	M 23	Portal cirrhosis	4·0	0·5	Absent	Splenorenal
2	M 52	,, ,,	3·1	1·2	,,	,,
3	M 53	,, ,,	3·7	1·6	,,	Portacaval
4	M 33	,, ,,	3·3	0·7	,,	Splenorenal
5	M 63	,, ,,	3·5	2·0	,,	,,
6	F 42	,, ,,	3·0	0·6	,,	,,
7	M 64	,, ,,	3·5	0·5	,,	Portacaval
8	F 59	,, ,,	2·4	0·3	,,	,,
9	M 36	,, ,,	3·3	0·6	,,	,,
10	M 37	,, ,,	3·6	0·7	,,	,,
11	F 57	,, ,,	3·2	0·4	,,	,,
12	F 42	,, ,,	2·9	0·3	,,	,,
13	F 42	,, ,,	2·8	0·7	,,	,,
14	M 49	,, ,,	3·0	0·4	,,	,,
15	F 68	,, ,,	2·4	0·4	,,	,,
16	F 71	,, ,,	3·8	0·9	Present	,,
17	M 57	,, ,,	3·7	1·3	Absent	,,
18	F 53	,, ,,	4·2	0·6	,,	,,
19	F 58	,, ,,	3·7	0·2	,,	Splenorenal
20	F 46	,, ,,	3·6	1·2	,,	Portacaval
21	F 67	,, ,,	3·1	0·5	,,	Splenorenal
22	F 58	,, ,,	3·1	0·5	,,	Portacaval
23	F 59	,, ,,	3·5	0·4	,,	,,
24	F 56	,, ,,	3·4	0·8	Present	Splenorenal
25	F 64	,, ,,	2·4	2·4	,,	Portacaval
26	F 57	,, ,,	3·5	0·8	Absent	,,
27	M 40	,, ,,	3·7	0·2	,,	,,
28	F 63	,, ,,	3·1	0·9	Present	,,
29	F 53	,, ,,	3·4	0·4	Absent	,,
30	F 54	,, ,,	2·7	2·5	Present	Splenorenal
31	M 40	,, ,,	4·3	0·2	Absent	Portacaval
32	M 46	,, ,,	4·5	0·4	,,	,,
33	F 74	Hydatid disease. Budd-Chiari syndrome	2·8	1·6	Present	Splenorenal

quantitative replacement of blood loss, planned anaesthesia, and careful post-operative care. The more theoretical aspects of the surgical care of patients with liver disease have been reported (Riddell and Jones, 1959), and although it is not our intention to review this again we describe our present programme for the care of these patients.

Pre-operative Care

The first essential of preoperative care is to bring liver function to the best achievable standard, and the main therapeutic weapon is a high-protein, high-calorie diet. This should be started with caution because of the danger of producing ammonia intoxication from high-protein feeding (McDermott, Adams, and Riddell, 1954). If the patient can tolerate it, the diet is increased to 120 g. of protein and 3,000 calories a day. Tube feeding, especially at night, is useful in patients with anorexia. Generous vitamin supplements are given, with the addition of vitamin K intramuscularly. In a few patients the level of the serum albumin has been raised by intravenous infusion of salt-free albumin with apparently beneficial results.

Haemoglobin deficits should be corrected before operation by transfusion with packed red cells. However, care is required as substantial increases in blood volume may raise the portal pressure and precipitate further haemorrhage. Attempts to increase the haemoglobin level above 10 g./100 ml. (70%) are inadvisable.

In the prevention of ammonia intoxication in the immediate post-operative period the patient is taken off his high-protein diet three days before operation. Two days before operation he is given 1 g. of neomycin orally every four hours, and this is continued for a week post-operatively. This reduces bacterial fermentation in the gut and consequently lowers the production of ammonia from the alimentary tract.

Care During Operation

Careful blood replacement is of the utmost importance during operations on patients with cirrhosis, for two reasons: firstly, oligaemia will result in hypoxia of the liver cells which may precipitate liver-cell necrosis; and, secondly, patients with liver damage are more liable to citrate intoxication than the normal patient, as the damaged liver is less able to deal with the citrate in the transfused blood. Quantitative replacement of any blood loss is therefore required. To achieve this the blood loss is continuously estimated by the technique of swab weighing and any deficit is immediately replaced.

Anaesthetic Technique

These patients tolerate hypotension and its attendant hypoxia badly, and every precaution should be taken to prevent it occurring, especially in the immediate post-operative period. It is therefore mandatory not to return these patients to the ward until any blood loss is replaced and the blood-pressure is restored to its preoperative level. These factors have become the guiding principles in the development of the anaesthetic technique.

In our early cases hypotensive anaesthesia was not employed to reduce bleeding, but in the second half of the series halothane has been used with increasing frequency to lower the systolic blood-pressure to between 80 and 100 mm. Hg. It is very difficult to define the degree of hypotension that is permissible and for how long it may be continued. At present we feel that the levels mentioned above are satisfactory, but the arterial pressure must be returned to its normal value before the end of the operation. Hypotensive anaesthesia, together with the employment of a positive/negative-phase respiratory pump, has reduced the bleeding from the operative field and the total blood loss has been approximately halved. Halothane produces marked vasodilatation, and with blood-pressures of the order mentioned above there is an efficient peripheral circulation. Although in some instances the administration of halothane has continued for four or five hours no adverse effect on liver function has been detected. By using halothane as an adjunct to nitrous oxide and oxygen it is possible to reduce the induction dose of thiopentone to the minimum, and the morphine group of drugs are unnecessary until the post-operative period.

Complete muscular relaxation is essential throughout the operation, and for this both suxamethonium chloride and D-tubocurarine have been used, but never both drugs in the same patient. Better relaxation is obtained with suxamethonium given intermittently, but the technique is tedious and the patient requires careful observation both to maintain full relaxation and to prevent an excess of the drug being given as the interval between successive doses increases. There has been no difficulty in establishing normal respiratory exchange at the end of operation. Neostigmine is always given after

D-tubocurarine in dosage sufficient to produce a normal tidal air. Whichever drug is used to produce relaxation it is essential to keep the patient on the respiratory pump until it is absolutely certain that the action of the relaxant has been completely reversed.

The use of a mechanical ventilator for long operations of this kind offers three main advantages: (1) it ensures even ventilation, which is necessary to maintain proper oxygenation and carbon dioxide elimination; (2) the regular rhythm of the pump is a great help when performing a difficult dissection in the hilum of the liver; and (3) the use of a negative-phase respirator reduces venous congestion and so bleeding.

The use of halothane with a respiratory pump is permissible only if the concentration of vapour in the inspiratory gases is accurately known and controllable. Probably the most economical technique is to pass 3–4 litres of 1% halothane per minute, using nitrous oxide and oxygen as a vehicle, into a non-return circuit and to make up the balance of the minute-volume with air. If the whole of the inspired gases are passed through a halothane vaporizer then concentrations of less than 0.5% must be used. Anaesthesia must be kept light enough for the patient to regain consciousness before he returns to the ward.

We make it a rule never to return a patient to the ward unless: (*a*) blood loss has been completely replaced; (*b*) blood-pressure is at its preoperative level; and (*c*) reflexes are present with a normal respiratory function—that is, respiratory exchange is sufficient to maintain full oxygenation without the aid of oxygen.

Post-operative Care

The immediate post-operative care of the patient is similar to that of any patient who has had a thoraco-abdominal incision. These patients tolerate all forms of sepsis badly, and it is important to get the lung expanded at the earliest possible moment and remove any retained secretions.

In patients with liver disease there are abnormalities of water and salt metabolism, and it is easy to produce water and sodium retention. It is our practice to give no sodium intravenously on the first post-operative day and to limit the intake of water to 1,000 ml. for this period. The gastric tube is removed on the second day, and shortly after this the intravenous infusion is discontinued. In a few patients 500 ml. of 0.9% NaCl has been given on the second day.

After surgery, protein feeding is resumed with caution during the fifth to seventh post-operative days. The diet is then built up in 10-g. increments every two days until 70 g. is reached. The protein intake is maintained at this level for three months before increasing it to 120 g. Increasing the dietary protein above 70 g. too soon after operation may precipitate portasystemic encephalopathy.

Summary and Conclusions

For the operation of portacaval and splenorenal anastomosis to be of value in the treatment of bleeding oesophageal varices the operative mortality must be low.

We report a series of 33 consecutive shunt operations without operative mortality.

The factors which are important in maintaining a low operative mortality are described.

References

Linton, R. R. (1951). *Ann. Surg.*, **134**, 433.
McDermott, W. V., Adams, R. D., and Riddell, A. G. (1954). Ibid., **140**, 539.
Nachlas, M. M. (1958). Ibid., **148**, 169.
Riddell, A. G., and Cassie, A. B. (1959). *Recent Advances in Surgery*, edited by S. Taylor, p. 437. Churchill, London.
—— and Jones, W. K. (1959). Ibid., p. 420.

ASPECTS OF CONVALESCENCE AFTER HERNIORRHAPHY

A REVIEW OF 762 PATIENTS

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The purpose of this investigation was to study the actual convalescence of patients treated at a general surgical hospital and to relate this to other factors affecting the results of operation. All operations for herniae performed at the Bolingbroke Hospital in the years 1948–57 have therefore been reviewed.

"Nobody seems to be able, or prepared, to answer the question: When shall a patient return to work? Perhaps this is because the convalescent is in a therapeutic no-man's-land." And, again, convalescence "is an aspect of hospital treatment which after 20 years remains almost unchanged" (*Lancet*, 1957).

The Oxford Dictionary defines convalescence as the period of regaining health, and one can therefore regard surgical convalescence as beginning as the operation ends. The concept of health is incapable of mensuration. So in discussing the problems of convalescence it is more profitable to consider two periods of time: firstly, the length of stay in hospital and/or convalescent home; and, secondly, the length of time between discharge and return to work or full activity.

In practice these periods are often a compromise between what the patient considers economically possible and what the physician considers ideally necessary. Although the former is beyond the scope of the present study, its importance is reflected in the results obtained in this series.

The length of convalescence considered desirable after individual operation is a subject which has received little study. Medical students are taught much about the criteria for operation, the methods of operation, and to a less extent about post-operative management. But authoritative guidance on the further stages is lacking. Each surgeon has his own views on how long he likes to keep his patients in bed post-operatively and whether or not they should spend a period of convalescence at a recognized home or hostel. But the time of return to work may be decided upon by the registrar or house-surgeon who sees the patient in the follow-up clinic, by the patient's own general practitioner, or even by the patient himself.

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Moss *et al.* (1957) drew attention to the diversity of views on the subject. They obtained 229 opinions (including those of professors of surgery, board certified general surgeons, industrial physicians, and general practitioners) on the convalescence desirable after four different common operations—namely, appendicectomy, haemorrhoidectomy, herniorrhaphy, and cholecystectomy.

In the case of herniorrhaphy, examples chosen were a man aged 25 and one aged 50, with an indirect inguinal hernia, otherwise healthy, of normal weight, and with no complications. The patient was assumed to return to the job which he had held for at least one year prior to operation. The lengths of convalescence suggested for the 50-year-old lay between 1 and 10 weeks for return to light work, and from two weeks to six months for heavy work. For the 25-year-old the figures were from 1 to 12 weeks and from 2 to 24 weeks respectively. The average time, taking both groups together, was 22 days for light work and 48 days for heavy work.

Saffeir (1958) investigated patients covered by insurance schemes paying for convalescence after operation. In men the average duration of convalescence after haemorrhoidectomy was three weeks, after appendicectomy three to four weeks, and after herniorrhaphy six weeks. There were large variations in both sexes, but all convalescences were longer in women. Men employed in heavy labour took twice as long to return to normal work as those in light work. The time taken over convalescence increased with age.

Herniorrhaphy is one of the commonest operations performed in our general hospitals. Over the past 10 years at the Bolingbroke Hospital, about 10% of all the operations performed were herniorrhaphies. The condition thus has some economic importance to the community, as well as to the individual. However, even in this common condition there is no unanimity concerning the period of convalescence.

Edwards (1943), in an authoritative survey, mentioned 22 possible operations, which is sufficient indication of the technical controversy. With regard to after-treatment he says: "The fact seems to be that if one excises the sac only, without interfering with the musculature, early ambulation does not have any malign influence, except that it goes counter to the sound and age-long practice of resting a wound till it has healed. If this operation is combined with careful repair of the transversalis fascia, then weight-bearing upon the scar should be avoided until the fascia has healed, and this is adjudged to take three weeks." For the inguinal region he recommended muscle exercises in bed from the eleventh day onward, three weeks in bed, and three to four weeks in a convalescent depot, where eventually the full range of physical training is practised. This was, in fact, the procedure adopted by the British Army during the late war.

In recent years the tendency has been towards earlier ambulation and, to a less extent, shorter convalescence, partly in an effort to reduce the incidence of deep vein thrombosis and pulmonary embolism and partly because of the demands on bed space.

Wenger (1956) reported on 639 herniorrhaphies on U.S.A.A.F. personnel, in which the average time lost from duty was only 19.9 days, with a recurrence rate of 4.25%. He concluded that this comparatively short period saved money and man-hours, while it did not affect the recurrence rate. This is admittedly a selected group of healthy young males.

Method of Investigation

A complete abstract on punch cards of the notes of all abdominal herniae operated upon from January 1, 1948, to December 31, 1957, was made.

A questionary was sent to each of the patients operated upon in the years under review. The patients were requested to complete these and bring them along when they attended hospital for examination for possible recurrence of the hernia. Those patients who for various reasons were unable to attend were asked to give their permission for a home visit. The questionary answers were checked at the hospital visit.

TABLE I.—*Analysis of Patients Seen by Year in Which Operation was Performed*

Year	Total No.	No. Dead	No. Seen	No. of Recurrences in Patients Seen
1948	119	8	77 (64·7%)	5
1949	98	9	55 (56·1%)	4
1950	73	7	49 (67·1%)	1
1951	89	4	56 (62·9%)	5
1952	109	5	80 (75·2%)	5
1953	82	4	62 (75·6%)	4
1954	121	5	98 (81%)	5
1955	108	7	88 (81·5%)	11
1956	112	3	100 (89·3%)	11
1957	107	3	97 (90·6%)	3
	1,018	55	762	54

Information Collected.—Out of 1,018 patients operated upon during the 10 years, 762 were personally seen and examined by one or both of us, 55 had died, and the remainder were untraceable despite exhaustive efforts (Table I). The 762 patients seen form the basis of this investigation.

Results

The information collected can be placed into four main categories for ease of comparison and correlation (Table II). Most of the information is factual. In this series the preoperative and operative factors varied greatly from year to year in a haphazard way. But many important factors concerning a patient and his hernia are imponderable. The assessment of these will vary with the criteria of the investigators. In a retrospective study, their importance must not be forgotten as a variable factor affecting the result obtained.

Table III analyses the type of hernia seen in each year under review. It is seen that the indirect hernia was the commonest, direct inguinal and femoral hernia were present in equal number, and umbilical and incisional herniae formed the smallest group seen.

Tables IV and V show respectively the time the patients were kept in bed and the time they spent in hospital. The trend is demonstrably towards a shorter time in bed and consequently a shorter period in hospital. Table VI shows that the percentage of complications was no higher in the earlier years of the study and therefore could not account for longer hospitalization.

Table VII shows the total time spent on convalescence—that is, from the date of operation to the date of return to work. Here the figures are roughly comparable for each year; so, presumably, in the earlier years the patients, although staying longer in hospital, spent a shorter period convalescing after discharge. That this is not due to variation in social status or physical activity of the patient is shown by Table VIII.

Table IX demonstrates that the nature of the patient's work does affect the length of convalescence. Thus only

42.4% of those engaged in heavy work had returned to work by six weeks against 72% in light work and 66% in sedentary occupations.

When length of convalescence is correlated with social status (Table X) it is found that less than half of those in class V have returned to work by six weeks, whereas over 60% of all other classes have returned by this time. This would be expected, as most of those engaged in heavy work are also in social class V.

TABLE II.—*Synopsis of Factual Information Which May be Collected from Patients with Abdominal Herniae*

1. *Preoperative factors:* Age and sex. Type of hernia. Method of admission (list or emergency). Length of history. Previous treatment.
2. *Operative factors:* Status and experience of surgeon. Type of operation. Suture material used for repair. Anaesthetic employed.
3. *Post-operative factors:* Time in bed post-operatively. Complications and intercurrent diseases. Post-operative treatment. Time in hospital. Time convalescent. Type of work and social status.
4. *Miscellaneous factors:* General condition and health of patient. Condition of musculature. Size of hernia. Decision and reason for return to work. Period of time between repair and review. Examination standard of recurrence.

TABLE III.—*Analysis of Type of Hernia Operated Upon (as Percentage of Total Seen at Follow-up)*

Year	Indirect Inguinal	Direct Inguinal	Femoral	Umbilical	Incisional	Other
1948	60	16·7	14·3	7·7	1·3	—
1949	61·8	16·4	10·8	5·5	5·5	—
1950	71·4	10·2	12·3	6·1	—	—
1951	64·3	10·7	16	7	1·7	—
1952	60	10	15	6·3	8·7	—
1953	51·6	21	22·6	4·8	—	—
1954	64	15·3	12·2	3·2	3·2	2·1
1955	58	18·2	12·4	6·8	4·6	—
1956	67	16	9	4	4	—
1957	64	13·4	14·4	4·2	3	1

TABLE IV.—*Time in Bed Post-operatively in Days (Expressed as Percentages of Those Patients Seen)*

Year	Days in Bed							
	1	2	3	4	5	6	7+	Not Known
1948	6·5%	6·5%	1·2%	3·8%	2·6%	1·2%	74·8%	3·4%
1949	9	—	9	3·6	7·2	1·8	56·7	12·7
1950	6·2	4·1	4·1	4·1	6·2	—	75·3	—
1951	23·2	8·9	10·1	3·5	8·9	7	34·3	3·5
1952	15	23·8	7·5	18·7	7·5	1·2	23·8	2·5
1953	1·6	4·8	6·3	12·9	9·6	—	60	4·8
1954	7	10·2	21·5	13·3	11·4	3·1	26·5	7
1955	13·6	18·2	7·9	5·6	18·2	4·7	28·4	3·4
1956	22	19	22	3	10	3	20	1
1957	44·5	15·5	17·6	2	3	3	11·4	3

TABLE V.—*Time in Hospital in Days (Expressed as Percentages of Those Patients Seen)*

Year	Days in Hospital				
	0–7	8–10	11–14	15–21	22+
1948	—	—	10·8%	75%	14·2%
1949	—	5·4	16·3	65·6	12·7
1950	2	8·1	18·3	59·4	12·2
1951	—	43·0	32·1	21·4	3·5
1952	—	27·5	38·7	25	8·8
1953	8	4·8	42·1	30·6	14·5
1954	8·3	5·1	32	29·3	5·1
1955	15	1·1	51	29·5	3·4
1956	5	4	55	26	10
1957	6·1	7·1	61	15·5	10·3

TABLE VI.—*Complications Seen in Patients Followed Up*

Year	Incidence of Complications	Chest Infection	Wound Haematoma	Wound Infection	Venous Thrombosis	Other
1948	12 (15·5%)	5	1	2	—	4
1949	4 (7·2%)	—	1	1	—	2
1950	7 (14·2%)	—	—	—	7	—
1951	6 (10·7%)	3	1	—	—	2
1952	18 (22·5%)	9	5	3	—	1
1953	14 (22·5%)	4	3	5	1	1
1954	26 (26·5%)	5	10	7	2	2
1955	11 (12·5%)	4	3	4	—	—
1956	13 (13%)	6	1	3	2	1
1957	23 (23·7%)	6	4	7	2	4

TABLE VII.—*Time Convalescent in Weeks in Patients Seen but Excluding Those Retired or Children at the Time of Operation (Expressed as a Percentage of Number Seen)*

Year	Weeks							Weeks	
	0–2	3–4	5–6	7–9	10–12	13–18	18+	0–6	7–18+
1948	4·8	28·5	33·3	17·4	8·0	3·2	4·8	66·6	33·4
1949	8·9	48·9	22·2	8·9	8·9	2·2	—	80	20
1950	6·6	34·7	21·7	15·2	6·6	8·6	6·6	63	37
1951	5·8	36·5	19·3	9·6	11·6	3·8	13·4	61·6	38·4
1952	12	34·8	27·2	6·5	9·0	7·5	3	74	26
1953	12	38	14	22	6	6	2	64	36
1954	6	31·4	26·5	19·3	4·8	3·6	8·4	63·9	36·1
1955	5·7	30·5	33·4	17·4	7·3	4·3	1·4	69·6	30·4
1956	6	22	22	18·3	18·3	7·4	6	50	50
1957	2·8	33·9	24	22·5	12·6	1·4	2·8	60·7	39·3

TABLE VIII.—*Social Status and Physical Activity of Those Patients Followed Up, Expressed as a Percentage of Those Seen*

Year	Social Status					Activity			
	I	II	III	IV	V	Heavy	Light	Sedentary	Retired
1948	5·2	11·7	35	28·6	19·5	20·8	61	15·6	2·6
1949	1·8	32·7	29	30·9	5·5	14·6	69·1	12·7	3·6
1950	6	14·2	34·8	24·6	20·4	18·6	67	10·3	4·1
1951	7	14·1	30·6	34·5	14·1	21·3	61·4	14·2	3·1
1952	6·2	13·7	20	45	15	13·7	62·5	18·8	5
1953	3·2	6·5	27·4	50	12·9	22·6	51·6	12·9	12·9
1954	10·2	10·2	27·5	36·7	15·4	20·4	46·9	22·5	10·2
1955	9·1	12·5	26·1	33	19·3	19·3	55·7	13·6	11·4
1956	6	10	31	36	17	17	58	9	16
1957	11·5	11·5	26·7	35	15·3	14·4	48·5	17·5	19·6

TABLE IX.—*Time Convalescent in Weeks in Patients Considered by Type of Work*

Work	No. of Cases	Weeks											
		0–2		3–4		5–6		7–12		13–18		18+	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Heavy	141	3	2·1	32	22·7	25	17·8	51	36·2	11	7·8	19	13·5
Light	395	40	10·1	136	34·4	110	27·8	86	21·8	16	4·1	7	1·8
Sedentary	99	6	6·1	36	36·3	23	23·2	26	26·2	3	3·0	5	5·0

TABLE X.—*Time Convalescent in Weeks in Patients Considered by Social Status*

Social Status	Weeks												Returned at 6 Weeks
	0–2		3–4		5–6		7–12		13–18		18+		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
I (49)	3	6·1	13	26·1	14	28·9	13	26·1	2	4·1	4	8·2	61%
II (79)	7	8·8	36	45·4	23	30·4	9	11·3	4	5·0	0		84%
III (184)	13	7·1	58	31·5	43	23·3	53	28·8	9	4·9	8	4·3	62%
IV (225)	23	10·2	78	34·7	53	23·6	55	24·4	8	3·5	8	3·5	68%
V (98)	3	3·1	19	19·4	25	25·4	33	34·1	7	7·2	11	11·4	48%

However, in relating the length of convalescence to age (Table XI) there are no striking differences in the percentages returning to work before and after six weeks' convalescence.

Similarly, there are no striking differences in the time taken to convalesce with respect to the type of hernia. Half to three-quarters of all patients return to work within six weeks of their operation (Table XII).

The recurrence rate, expressed as the percentage of recurrences per number of patients seen for each convalescent period, is shown in the Chart. It is seen to vary haphazardly, and therefore no conclusion can be drawn other than that a short convalescence does not appear to influence recurrence.

Perhaps the most striking finding in this investigation is the reason given by the patients for their return to work (Table XIII). The columns refer to the person who first suggested return to work, and it is remarkable that in two-thirds of the cases it is the patient.

TABLE XI.—*Time Convalescent in Weeks in Patients Considered by Age, Expressed in Actual Number Seen in Each Group (Excluding Patients Retired and Children)*

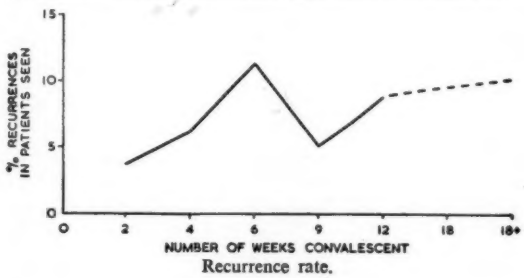
Age	Weeks 0–2		3–4		5–6		7–12		13–18		18+		Returned at 6 weeks
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
10–19 (12)	—		7	58·3	—		1	8·3	1	8·3	3	24·9	58·3%
20–29 (52)	6	11·5	17	32·7	13	25·0	12	23·0	2	3·8	2	3·8	69%
30–39 (108)	11	10·2	38	35·2	30	27·7	19	17·6	3	2·8	7	6·5	73%
40–49 (193)	14	7·2	60	31·1	50	25·8	47	24·3	13	6·7	9	4·6	64%
50–59 (168)	7	4·2	47	28	42	25·1	58	34·5	7	4·2	7	4·2	57%
60–69 (79)	6	7·6	26	32·9	20	25·3	21	26·6	4	5·1	2	2·5	65·8%
70–79 (23)	5	21·5	9	39·1	3	13·0	5	21·5	—		1	4·3	73%

TABLE XII.—*Time Convalescent in Weeks in Patients Seen—Excluding Patients Retired and Children at Time of Operation—According to Type of Hernia*

Type of Hernia	Weeks 0–2	3–4	5–6	7–12	13–18	18+	0–6
	%	%	%	%	%	%	%
Indirect inguinal	6	31·4	25	27·8	4	5·8	62·4
Direct "	2·8	30	30	25·7	7·7	3·8	62·8
Femoral " ..	18·1	35·1	22·4	18·1	4·2	2·1	75·6
Incisional ..	13·0	34·8	17·4	30·4	—	4·4	65·2
Umbilical ..	11·5	19·3	23·1	23·1	11·5	11·5	53·9

TABLE XIII.—*Reason Stated by Patients Interviewed for Return to Work, Excluding Patients Retired or Children*

Year	Own Wish	Own Doctor's Instructions	Hospital Doctor's Instructions	Works Doctor's Instructions
1948	65	23·8	8	3·2
1949	76·5	23·5	—	—
1950	60	35·6	2·2	2·2
1951	71·2	17·3	7·7	3·8
1952	70·2	19·4	10·4	—
1953	64	18	6	12
1954	58	27·6	9·6	4·8
1955	66	23·8	10·4	5·8
1956	65·5	14·8	12·3	7·4
1957	60	26·3	9·5	4·2



Recurrence rate.

Discussion

In any discussion on convalescence it is realized that there are innumerable factors which will play a part in deciding the time actually taken to convalesce by any one patient. Table II is an attempt to list and clarify some of these points, which also have an equal bearing on recurrence of a hernia.

Most of the preoperative, operative, and post-operative factors can be factually reported. It was noted in this series that in every year there was a great diversity in all these factors, which did not follow any set pattern. But among the miscellaneous factors listed, certainly the decision to return to work cannot be evaluated, especially when it is realized that the majority of patients make up their own minds, apparently uninfluenced by their medical advisers. This is a salutary lesson. It is presumed that the decision is made when the patient feels able and fit to resume his occupation. Economic factors are doubtless of importance.

The observed result is that the majority of patients will return to work within six weeks. In 8 out of the ten years and in all but umbilical herniae, the highest number had only six weeks' convalescence from the date of operation. This means that most patients take only four weeks' rest at home. This appeared to have no malign effect upon the recurrence rate.

The length of convalescence did not vary with age or type of hernia. However, there was a tendency, as one would expect, for those patients in the lowest social class and performing the heaviest work to take longer over their convalescence. The incidence of recurrence of herniae in those cases seen did not vary significantly from year to year.

Summary

A review of 762 herniae is presented.

The diversity of factors involved in the treatment of herniae is discussed. The convalescent period is shown to be directly determined by the patient in the majority of cases. Most patients favour a period of two to four weeks (four to six from date of operation) after various types of hernia repair. This period is unrelated to age, type of hernia, work, or social status, except in class V and the heaviest work, but does vary as expected with the occurrence of complications.

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REFERENCES

Edwards, H. C. (1943). *Brit. J. Surg.*, **31**, 172.
Lancet, 1957, **2**, 1269.
Moss, N. H., Schwegman, C. W., and Dohan, F. C. (1957). *J. Amer. med. Ass.*, **165**, 322.
Saffeir, H. J. (1958). *Ann. N.Y. Acad. Sci.*, **73**, 444.
Wenger, D. S. (1956). *Industr. Med.*, **25**, 307.

A CLINICAL STUDY OF SERUM ANTINUCLEAR FACTOR

BY

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Since the description of the L.E.-cell phenomenon by Hargraves *et al.* (1948) and the rheumatoid factor by Rose *et al.* (1948) and Waaler (1940), immunological abnormalities in the connective-tissue diseases have been extensively sought for and studied.

In sera from patients with systemic lupus erythematosus (S.L.E.) a number of abnormal globulin factors have now been described, including autoimmune haemolytic antibodies (Zoutendyk and Gear, 1950), antiplatelet and anticoagulation factors (Dameshek, 1958; Loeliger, 1959), antileucocyte agglutinations (Seligman, 1958), and anticytoplasmic complement-fixing antibodies (Mackay and Gajdusek, 1958; Asherson, 1959; Deicher *et al.*, 1960).

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After the localization of the L.E.-cell factor in the γ-globulin fraction of serum by Haserick *et al.* (1950), Miescher (1957) used the antiglobulin consumption test to demonstrate the affinity of this factor for cell nuclei, and since then a number of other techniques have been used to show serum reactions with nuclear material, including the fluorescent antibody technique (Friou *et al.*, 1957, 1958; Holborow *et al.*, 1957; Holman and Kunkel, 1957; Alexander and Duthie, 1958), complement fixation (Ceppellini *et al.*, 1957; Pearson *et al.*, 1958; Seligman, 1958), precipitation (Ceppellini *et al.*, 1957; Seligman, 1958), haemagglutination (Miescher and Strässle, 1957; Goodman and Bowser, 1958; Lee and Epstein, 1960), and latex precipitation (Christian *et al.*, 1958; Fessel, 1959).

This paper is concerned with the serum antinuclear factor, which we have previously reported (Holborow *et al.*, 1957), and presents a study of its distribution in systemic lupus erythematosus, rheumatoid arthritis, and some other conditions.

Materials and Methods

The demonstration of the antinuclear serum factor utilizes Coons's indirect technique, in which globulin uptake by tissue sections is demonstrated by treatment with anti-human-globulin serum conjugated with fluorescein isocyanate or isothiocyanate. Sections pretreated with serum containing antinuclear factor (A.N.F.) show bright overall apple-green fluorescence of the cell nuclei (Holborow *et al.*, 1957) when viewed microscopically by ultra-violet light, whereas control sections pretreated with normal serum show no fluorescent staining.

Preparations of Tissue Sections.—The selection of cell nuclei in a suitable form for the test is an important consideration. Preparations of nuclei which we have tested include smears of cell nuclei prepared from tissue homogenates, human leucocyte films, and monolayers of cells grown in tissue culture. None of these preparations was ideal owing to non-specific uptake of serum protein, which leads either to excessive background staining or sometimes to non-specific nuclear staining. Experience with tissue-culture monolayers indicated the need for some cell damage before the nuclei could take up the serum factor. Freezing and thawing gave suitable preparations, but mild trypsinization resulted in considerable non-specific protein uptake by the cells. The most satisfactory nuclear preparations for routine use were made from thyroid tissue because of the orderly and predictable arrangement of the cell nuclei, and this tissue was used for the present study. Human infant thyroid tissue was preferred to adult tissue, because the latter usually contains numerous autofluorescent granules in the epithelial cytoplasm, and much interstitial autofluorescent collagen, both of which interfere with observation of the sections. Human neonatal thyroid from very fresh post-mortem specimens was cut into small blocks and instantly frozen in a sealed container in solid carbon dioxide and alcohol mixture (approximately −70° C.), transferred to a freezing cabinet at −20° C., and stored without thawing. Sections were cut in a cryostat chamber on a microtome at 6 μ and mounted on slides and dried as described by Coons and Kaplan (1950). Each section was covered with a few drops of test serum and incubated in a moist chamber at 37° C. for 30 minutes. After incubation the serum was carefully washed off in two changes of buffered saline (*p*H 7) for 20 minutes, fixed in 90% alcohol for five minutes, washed again and stained with a fluorescent conjugate prepared from anti-human-globulin serum. After 30 minutes the sections were again washed and mounted in buffered glycerin (*p*H 7).

Preparation of Conjugates. — The anti-human-globulin sera were prepared in rabbits by intravenous injection of rabbit red cells coated with human globulin (Milgrom *et al.*, 1956). Alternatively a horse anti-human whole serum obtained from the Pasteur Institute was used. The globulin fraction was precipitated from the antiserum by 50% saturation with ammonium sulphate, and conjugated according to the methods of Coons and Kaplan (1950) or of Marshall *et al.* (1958). To reduce non-specific staining conjugates were absorbed with rabbit-liver suspension. This is particularly important, as background fluorescence makes differentiation between stained nuclei and the stained background difficult. Anti-human-globulin-fluorescein conjugates vary in their ability to detect traces of serum protein remaining adherent to treated washed tissue sections, and this can sometimes lead to quite considerable background fluorescence in preparations treated with all normal sera. The staining in these cases may include "outlining" of the cell nuclei, which leads to difficulty in interpreting the A.N.F. test. The majority of tests reported here were carried out using a conjugate which did not show this effect. Tests using other conjugates were standardized where necessary by diluting sera 1 in 5 or 1 in 10 with saline. At this dilution standard normal sera gave minimal background fluorescence of the type described. The overall nuclear fluorescence acceptable as positive in the test is thus easily recognized.

Controls.—Each series of tests included a known positive and a known negative serum control. The specificity of the conjugate was controlled by inhibition of staining by unconjugated antiglobulin and the absence of similar staining by fluorescent conjugates with different specificities.

Ultra-violet Microscopy.—A Cook, Troughton, and Simms microscope unit (M2150) with dark-ground condenser (M1396) was used. The light source was a 250-watt mercury-vapour lamp with choke and switchgear (M1684).

L.E.-cell Test.—This was the clot method of Zimmer and Hargraves (1952) when fresh blood was available, or the indirect technique of Schultz *et al.* (1955) when serum only was available.

Selection of Sera

Systemic Lupus Erythematosus.—We have tested sera from 58 cases of S.L.E. diagnosed according to the criteria shown in the Appendix. This group consisted of 14 patients from this unit (Professor Bywaters), 12 patients from the Middlesex Hospital (Dr. Doniach), and 32 patients from the University Hospital, Leyden (Dr. Hijmans). In all these cases a positive L.E.-cell phenomenon had been demonstrated on one or more occasions. Five other Taplow cases which fitted the diagnostic criteria, but with negative L.E.-cell tests, were also included in the study.

Rheumatoid Arthritis.—This group was selected using the American Rheumatism Association criteria for diagnosis, and was from cases seen at this unit and

TABLE I.—*Antinuclear Factor in Sera of Cases of Liver Disease*

	No. Tested	A.N.F.-positive
Post-infective cirrhosis	9	4 (1 L.E.-cell positive)
Portal cirrhosis	4	1
Juvenile ,,	10	0
Alcoholic ,,	4	0
Primary biliary cirrhosis	3	0
Other types of ,,	9	0
	39	5

TABLE II.—*Distribution of Positive A.N.F. and L.E. Tests in Disease Groups Studied*

Diagnosis	A.N.F. No. Tested	A.N.F. Positive No.	A.N.F. Positive %	L.E. Cells No. Tested	L.E. Cells Positive No.	L.E. Cells Positive %
S.L.E.	63	62	98	63	58	92
Discoid lupus erythematosus	75	10	13	75	0	0
Rheumatoid arthritis	132	19	14	95	3	3
Still's disease	100	13	13	60	1	2
Thyroid ,,	110	14	13	107	0	0
Liver ,,	39	5	13	39	1	3
Rheumatic fever	56	0				
Pulmonary tuberculosis	65	2				
Scleroderma	8	0				
Dermatomyositis	4	2				
Paget's disease	4	1				
Normal sera	133	2				

Hammersmith Hospital, many of which were undergoing long-term follow-up (Dr. Dixon and Professor Bywaters).

Still's Disease.—The cases were seen at this unit (Ansell and Bywaters, 1959).

Discoid Lupus Erythematosus.—Sera came from L.E.-cell-negative patients without signs of systemic disease (Scott and Rees, 1959).

Liver Disease.—This group of sera came from patients in Hammersmith Hospital and from Hamburg (Dr. Dölle). These patients are classified in Table I.

Results

Table II shows the results of A.N.F. and L.E.-cell tests on the sera from the cases described above. All 58 cases of systemic lupus with positive L.E.-cell tests gave positive A.N.F. tests at first testing, and none became negative subsequently. Four of the five L.E.-cell-negative S.L.E. cases were positive for A.N.F. and one was negative despite repeated testing. This case was that of a 21-year-old woman presenting six years ago with typical butterfly rash, loss of weight, pyrexia, loss of hair, generalized lymphadenopathy, splenomegaly, arthralgia, and leucopenia. Three years ago the E.S.R. returned to normal, and on steroid therapy she apparently recovered. Repeated tests for L.E. cells throughout her illness and (during the last three years) for A.N.F. have been negative.

In the rheumatoid arthritis group of 132 cases, 19 gave a positive A.N.F. test. Two of these were L.E.-cell positive and 17 were negative, but a third L.E.-cell-positive case was encountered which was persistently negative for A.N.F. In the group with Still's disease approximately the same incidence (13%) of positives was found.

The liver-disease group included nine cases of post-infective cirrhosis, and four out of the five positive A.N.F. tests occurred in sera from cases with this diagnosis. One of these four also gave a positive L.E.-cell test, another had haemolytic anaemia, and three out of the four had arthropathies. Joint involvement was present in only two out of the 34 A.N.F.-negative cases.

Positive A.N.F. tests have also been found in a significant percentage of cases of thyroid disease, including Hashimoto's thyroiditis and thyrotoxicosis. This group will form the subject of another communication (Hijmans, Doniach, Roitt, and Holborow, to be published).

Apart from these, we have found only five other cases positive for A.N.F. among the cases shown in Table II. These were two cases of clinical dermatomyositis from this unit, one case of Paget's disease with congestive failure, and two cases of pulmonary tuberculosis, one with penicillin hypersensitivity (in which the A.N.F. titre was low). Two other cases of drug sensitivity were negative. We also found two positives among 133 sera from apparently normal individuals. Both of these were weakly positive, with titres no higher than 1/10. It will be seen that in 63 other cases of pulmonary tuberculosis, and in 56 cases of rheumatic fever (active and quiescent), no positive tests were encountered. We have also tested 56 miscellaneous hospital cases, including chronic bronchitis, coronary disease, pneumonia, congestive cardiac failure, asthma, and iron-deficiency anaemia, none of which gave positive tests.

Serum Titrations.—Titration of A.N.F. by serial dilution in saline was carried out in 36 cases, testing for A.N.F. under standard conditions using the same tissue and conjugate. The sera chosen for this investigation were selected from the four main diagnostic categories in which the factor has so far been found. Table III

TABLE III.—*Titration of Antinuclear Factor*

	No. Tested	No. Positive at Stated Dilution: Neat—1/10	1/20–1/100	>1/100–1/300
S.L.E.	14		6	8
Rheumatoid arthritis	12	1	9	2
Liver disease	4		4	0
Thyroid ,,	6*	1	5	0
Dermatomyositis	1		1	0
Pulmonary tuberculosis	2	2	0	0
Normal sera (positives)	2	2	0	0

*Drs. Doniach and Roitt's cases.

gives the distribution of the titres according to the diagnosis, and shows that with two exceptions only S.L.E. sera could be diluted over 1/100 and still retain the ability to give a positive A.N.F. test. The low-titre group included some S.L.E. cases, most of the rheumatoid arthritis cases, and all the cases of liver and thyroid disease. Only four sera, in addition to the two normal sera described above, had titres of less than 1/10—one case of rheumatoid arthritis, one case of thyroid disease, and the two cases of pulmonary tuberculosis.

Discussion

The L.E.-cell phenomenon, which occurs in S.L.E. and sometimes in other diseases, has been shown to involve a serum factor reacting with nuclear material (Miescher and Fauconnet, 1954; Hijmans and Schuit, 1958). It is therefore possible that the antinuclear factor which we have described above represents the same serum factor. Our work does not enable us to draw any final conclusions on this point, because in many of the cases studied only serum, not fresh blood, was available, and therefore it was often possible to carry out L.E.-cell tests only by an indirect method. Studies which have revealed a high incidence of positive L.E.-cell tests in rheumatoid arthritis, for example, have used a sensitive direct method for the L.E.-cell test (Kievits *et al.*, 1956). In our hands, nevertheless, A.N.F. has had a much wider incidence in the disease groups studied than positive direct L.E.-cell tests. Thus, of the 19 rheumatoid arthritis patients positive for A.N.F.,

only two gave positive L.E.-cell tests by the direct method. In this group, however, titration of the A.N.F. in L.E.-cell-negative cases, where it was carried out, showed a low titre. On the other hand, we have encountered sera with A.N.F. titres of 1/100 where direct L.E.-cell tests were negative. Occasionally we have failed to find A.N.F. in sera from cases giving positive L.E.-cell tests, as in the rheumatoid arthritis case described above. Marmont (1959), however, has suggested that, in rheumatoid arthritis especially, apparently typical L.E. cells may sometimes be found in the absence of a specific serum factor, and it is possible that this L.E.-cell-positive and A.N.F.-negative case may belong to this category.

The significance of A.N.F. in the disease groups studied may be considered under two headings—diagnosis and aetiology.

Our results show that A.N.F. was present in all our cases of clinically definite S.L.E., except one in prolonged remission, discussed above. The difficulty of diagnosing borderline cases (particularly in the absence of L.E. cells) makes it impossible to assert that A.N.F. is present from an early stage in every case of the disease. Our experience indicates that once the factor has been found in S.L.E. it is likely to be continuously present thereafter, and its high correlation with proved S.L.E. makes this diagnosis unlikely in its absence. A positive test (as already indicated) is not by itself diagnostic of S.L.E.

Because of its antibody-like nature A.N.F. may be classed with the autoimmune phenomena characteristic of systemic lupus. If we accept A.N.F. as an indicator of autoimmune processes, its occurrence in some cases of discoid lupus confirms the aetiological relationship between this and the systemic form of the disease. In the same way the incidence of A.N.F. which we have found in the adult and juvenile forms of rheumatoid arthritis, while it may not indicate the true incidence because of case-selection factors, nevertheless suggests that an immunological abnormality comparable to that found in S.L.E. may exist also in rheumatoid arthritis. The finding of A.N.F. in cases of liver disease accords well with the work of Mackay and Gajdusek (1958), showing that in certain forms of cirrhosis autoimmune complement-fixing antibodies (A.I.C.F.) and L.E. cells may be found. It is possible here, however, that disordered serum-protein synthesis rather than an initial autoimmune disturbance may give rise to these findings.

The role of these "auto-antibodies" in the pathogenesis of S.L.E. is doubtful. The fact that infants of lupus mothers do not develop the disease despite the presence in their circulation at birth of L.E.-cell factor (Bridge and Foley, 1954), and that an S.L.E.-like disease and associated conditions occur in agammaglobulinaemic individuals (Good, 1960), suggests that circulating antibody alone cannot be responsible for the pathology of the disease.

The abnormality of the immunological mechanisms in S.L.E. responsible for the wide range of auto-antibody γ-globulin found in this condition is not understood, but the lack of organ specificity (and indeed of species specificity) shown by many of the auto-antibodies (including A.N.F.) which occur in this disease appears to distinguish it broadly from autoimmune states such as thyroiditis, encephalomyelitis, and aspermatogenesis.

The production of these auto-antibody factors in S.L.E. can be regarded as a breakdown in immune tolerance to the body's own tissue antigens. Thus Burnet (1959) envisages development of clones of antibody-forming cells capable of reacting with self, owing to a poorly functioning homoeostatic mechanism failing to suppress such mutant cells. If such malfunction were marked it would be likely, as Burnet suggests, to lead to a multiplicity of antibodies accompanying the emergence of many "forbidden clones." In rheumatoid arthritis, however, one may postulate that the abnormality is less marked and that the homoeostatic mechanism is less affected. In these circumstances only a limited number of forbidden clones emerge, and, so far as antinuclear factor is concerned, in only a proportion of cases. If we accept this view, it seems reasonable at present, on the basis of A.N.F. activity, to regard rheumatoid arthritis as a disease immunologically related to S.L.E.

Summary

Serum antinuclear factor (as shown by Coons's fluorescent antibody method) has been found in 62 out of 63 cases of systemic lupus erythematosus and in over 10% of cases of discoid lupus erythematosus, rheumatoid arthritis (including Still's disease), and liver disease. The nature of the factor is discussed in the light of current concepts of autoimmunity.

We are grateful to Professor E. G. L. Bywaters for help in the preparation of this paper, and for providing, with Dr. B. M. Ansell and Dr. Allan Dixon, many of the cases we have studied. Our thanks are also due to Dr. Deborah Doniach, of the Middlesex Hospital, and Dr. W. Hijmans, of the Rheumatology Department, University Hospital, Leyden, The Netherlands, for making available sera and clinical information from their cases of systemic lupus. Dr. Allene Scott and Dr. E. G. Rees, of St. Bartholomew's Hospital, kindly provided sera from their cases of discoid lupus, and Dr. W. Dölle from cases of liver disease.

APPENDIX. CRITERIA FOR SELECTION OF CASES OF LUPUS ERYTHEMATOSUS

Obligatory.—The sedimentation rate must be above 20 mm. in one hour, Westergren or Wintrobe.

Major Criteria.—(1) Rash compatible with disseminated lupus. (2) Leucopenia below 5,000. (3) Finding of L.E. cells in 15-minute search of one slide.

Minor Criteria.—(1) Arthralgia or effusions into joints. (2) Serositis. (3) Fever above 99° F. (37.2° C.) twice in 24 hours. (4) Retinal changes. (5) D.A.T. 1:16 or more. (6) Albuminuria above 5 mg./100 ml.

For the admission diagnosis the patient must have the obligatory criterion, plus two or more major criteria, *or* the obligatory criterion, plus one major and at least two minor criteria. These criteria were those submitted by Bywaters and Ansell to the M.R.C. Collagen Panel, 1952.

REFERENCES

Alexander, W. R. M., and Duthie, J. J. R. (1958). *Brit. med. J.*, **2**, 1565.
Ansell, B. M., and Bywaters, E. G. L. (1959). *Bull. rheum. Dis.*, **9**, 189.
Asherson, G. L. (1959). *Brit. J. exp. Path.*, **40**, 209.
Bridge, R. G., and Foley, F. E. (1954). *Amer. J. med. Sci.*, **227**, 1.
Burnet, F. M. (1959). *The Clonal Selection Theory of Acquired Immunity*. Cambridge Univ. Press.
Ceppellini, R., Polli, E., and Celada, F. (1957). *Proc. Soc. exp. Biol. (N.Y.)*, **96**, 572.
Christian, C. L., Mendez-Bryan, R., and Larson, D. L. (1958). Ibid., **98**, 820.
Coons, A. H., and Kaplan, M. H. (1950). *J. exp. Med.*, **91**, 1.
Dameshek, W. (1958). *Ann. intern. Med.*, **48**, 707.
Deicher, H. R. G., Holman, H. R., and Kunkel, H. G. (1960). *Arth. and Rheum.*, **3**, 1.
Fessel, W. J. (1959). *Ann. rheum. Dis.*, **18**, 255.

Friou, G. J., Finch, S. C., and Detre, K. D. (1957). *Fed. Proc.*, **16**, 413.
—— —— —— (1958). *J. Immunol.*, **80**, 324.
Good, R. A. (1960). In *Cellular Aspects of Immunity*, edited by G. E. W. Wolstenholme and Maeve O'Connor, p. 446. Ciba Foundation Symposium. Churchill, London.
Goodman, H. C., and Bowser, R. (1958). *Fed. Proc.*, **17**, 56.
Hargraves, M. M., Richmond, H., and Morton, R. (1948). *Proc. Mayo Clin.*, **23**, 25.
Haserick, J. R., Lewis, L. A., and Bortz, D. W. (1950). *Amer. J. med. Sci.*, **219**, 660.
Hijmans, W., and Schuit, H. R. E. (1958). *Vox Sang (Basel)*, **3**, 184.
Holborow, E. J., Weir, D. M., and Johnson, G. D. (1957). *Brit. med. J.*, **2**, 732.
Holman, H. R., and Kunkel, H. G. (1957). *Science*, **126**, 162.
Kievits, J. H., Goslings, J., Schuit, H. R. E., and Hijmans, W. (1956). *Ann. rheum. Dis.*, **15**, 211.
Lee, R. C., and Epstein, W. V. (1960). *Arthr. and Rheum.*, **3**, 41.
Loeliger, A. (1959). *Thromb. Diath. haemorrh. (Stuttg.)*, **3**, 237.
Mackay, I. R., and Gajdusek, D. C. (1958). *Arch. intern. Med.*, **101**, 30.
—— Taft, L. I., and Cowling, D. C. (1959). *Lancet*, **1**, 65.
Marmont, A. (1959). In *Immunopathology*, edited by P. Grabar and P. Miescher, p. 479. Basle.
Marshall, J. D., Eveland, W. C., and Smith, C. W. (1958). *Proc. Soc. exp. Biol. (N.Y.)*, **98**, 898.
Miescher, P. (1957). *Hautarzt*, **8**, 502.
—— and Fauconnet, M. (1954). *Experientia (Basel)*, **10**, 252.
—— and Strässle, R. (1957). *Vox Sang (Basel)*, **2**, 283.
Milgrom, F., Lusczynski, T., and Dubiski, S. (1956). *Nature (Lond.)*, **177**, 329.
Pearson, C. M., Craddock, C. G., and Simmons, N. S. (1958). *J. Lab. clin. Med.*, **52**, 580.
Rose, H. M., Ragan, C., Pearce, E., and Lipman, M. O. (1948). *Proc. Soc. exp. Biol. (N.Y.)*, **68**, 1.
Schultz, I., Baum J., and Ziff, M. (1955). Ibid., **88**, 300.
Scott, A., and Rees, E. G. (1959). *Arch. Derm.*, **79**, 422.
Seligman, M. (1958). *Rev. franç. Ét. clin. biol.*, **3**, 558.
Waaler, E. (1940). *Acta path. Microbiol. scand.*, **17**, 172.
Zimmer, F. E., and Hargraves, M. M. (1952). *Proc. Mayo Clin.*, **27**, 424.
Zoutendyk, A., and Gear, J. H. S. (1950). *Brit. med. J.*, **2**, 1175.

PURE RED-CELL APLASIA IN MARASMUS AND KWASHIORKOR TREATED WITH RIBOFLAVINE*

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During an investigation of the anaemias in marasmus and kwashiorkor it was found that a considerable proportion of patients developed pure red-cell aplasia or hypoplasia during treatment.

So far selective red-cell aplasia has not been reported as a complication of marasmus and kwashiorkor, perhaps because critical haematological work and bone-marrow cytology have not been extensively done in these conditions, and serial bone-marrow punctures are not commonly performed on small infants. As the aplasia does not usually develop until two weeks or more after admission, a single marrow examination done at that stage, when red-cell precursors are usually high, will not reveal a hypoplasia that is yet to appear.

From the present investigation it seems that this type of aplasia is a fairly common accompaniment of marasmus and kwashiorkor in Kenya, since it developed in nine instances during the treatment of 23 cases; of these, five were thoroughly investigated.

Red-cell aplasia probably has a number of different causes among which are thymomas (Chalmers and Boheimer, 1954; Jacobs *et al.*, 1959; Freeman, 1960), toxic agents, allergy, iso-immunization, and infections (Foy and Kondi, 1953).

The case of pure red-cell aplasia previously reported (Foy and Kondi, 1953) and successfully treated with riboflavine induced us to try this vitamin in the present cases, and the results are reported here.

Material and Methods

Typical cases of marasmus and kwashiorkor attending the King George VI Hospital, Nairobi, were diagnosed clinically by the criteria of Dean and Schwartz (1953), Scrimshaw *et al.* (1957), and Jelliffe and Dean (1959). On admission complete haematological and parasitological examinations were done, together with *x*-ray examination to discover any chest infection.

All cases were then admitted to the children's ward, where dietary treatment consisted of "casilan," skimmed milk, and vegetable oil mixture (Jelliffe and Dean, 1959). They were covered during the first week with either tetracycline or penicillin and streptomycin. Intercurrent infections, such as hookworm, giardiasis, malaria, measles, diarrhoea, and respiratory complaints, when present, were appropriately treated. As most of the patients had low haemoglobin (Hb) and mean corpuscular haemoglobin concentration (M.C.H.C.) levels, oral iron was given in appropriate doses.

Blood was taken from the internal jugular vein, and bone-marrow from the lumbar spinous processes. Blood and marrow examinations were done on admission and thereafter fortnightly, or more often, for from two to four months. Marrow iron was estimated by the direct unstained method (Rath and Finch, 1948; Wallerstein and Pollycove, 1958) and graded accordingly. For sideroblast estimations marrow smears were fixed with 10% formalin in absolute alcohol, washed in water, and the slide flooded with warm potassium ferrocyanide in 5N HCl, again washed in water and counterstained with 1% aqueous safranine. In searching for the red-cell precursors marrow particles were most carefully examined after staining with Leishman and Giemsa. Haemoglobin was determined by the cyanomethaemoglobin method, and the packed cell volume (P.C.V.) by the microhaematocrit. The proteins were estimated by the biuret method (Gornall *et al.*, 1949); fractionation was done by using 27.2% sodium sulphate, to avoid carrying over α_1-globulin to the albumin and thereby giving falsely high albumin and low globulin values. Separation of the globulins was done by low-voltage paper electrophoresis at constant *p*H to reduce the albumin trail. Since there were great variations in the protein content of the serum, sometimes falling as low as 3 g./100 ml. of total protein, the amount of serum seeded on to the paper was calculated by the formula

$$\mu l. = \frac{35}{T.P.}$$

Case Histories: Treatment and Results

Case 1

A 12-months-c[illegible] girl entered hospital on April 30, 1960, with typical [illegible] kwashiorkor and a three-months history of diarrhoea. [illegible] contained giardia; treated with mepacrine. Hb, [illegible] ml.; P.V.C., 33%;

0			
0			
0		11,000	4,580

*Riboflavine used in this work was kindly supplied by Roche Products Ltd.

W.B.C., 9,900/c.mm.; total proteins (T.P.), 3 g./100 ml.; albumin (A), 1.04 g./100 ml.; marrow haemosiderin (Fe), lumps grade 4; sideroblasts (sids.), 70%; giant stab-cells (G.S.C.), for which folic acid and vitamin B_{12} were given; red-cell precursors (R.C.P.), 17%.

May 20: Hb, 8.5 g./100 ml.; P.C.V., 31%; W.B.C., 6,700/c.mm.; T.P., 5.5 g./100 ml.; A., 2.04 g./100 ml.; marrow Fe, few lumps grade 2; sids., 0%; R.C.P., 38%.

May 23: Measles.

June 11: Child recovered from measles; severe diarrhoea; temperature 102° F. (38.9° C.); given sulphonamides, penicillin, and streptomycin. Hb, 9.4 g./100 ml.; P.C.V., 35%; W.B.C., 7,900/c.mm.; T.P., 6.5 g./100 ml.; A., 2.2 g./100 ml.; marrow Fe, big lumps grade 1; sids., 0%; R.C.P., 11%.

June 24: Diarrhoea better. Hb, 9.4 g./100 ml.; P.C.V., 35%; W.B.C., 8,400/c.mm.; T.P., 6.8 g./100 ml.; A., 3.5 g./100 ml.; marrow Fe, grade 1; sids., 0%; R.C.P., 32%.

July 11: Hb, 9.4 g./100 ml.; P.C.V., 35%; W.B.C., 6,600/c.mm.; T.P., 6.7 g./100 ml.; A., 3.1 g./100 ml.; retics., 0%; marrow Fe, lumps grade 1; sids., 0%; R.C.P., 0%.

July 18: Hb, 8 g./100 ml.; retics., 0%; marrow Fe, grade 1; sids., 0%; R.C.P., 0%. As there was complete red-cell aplasia of the marrow on two consecutive examinations, and the Hb was falling, riboflavine 5 mg. daily intramuscularly for six weeks was given.

July 25 and 28: Retics., 1% and 9%.

August 2: Hb, 8.8 g./100 ml.; P.C.V., 33%; W.B.C., 18,000/c.mm.; T.P., 6.8 g./100 ml.; A., 3.1 g./100 ml.; marrow Fe, nil; sids., 4%; R.C.P., 25%.

August 16: Hb, 10.5 g./100 ml.; P.C.V., 38%; W.B.C., 10,200/c.mm.; T.P., 7.8 g./100 ml.; A., 3.5 g./100 ml.; sids., 29%; R.C.P., 17%.

August 29: Hb, 11.7 g./100 ml.; P.C.V., 43%; discharged from hospital.

Case 2

A 1-year-old Kikuyu girl entered hospital on March 30, 1960, with typical marasmus/kwashiorkor, and a six-months history of diarrhoea and cough. *X*-ray examination showed miliary tuberculosis; treated with streptomycin and isoniazid. Hb, 9.4 g./100 ml.; P.C.V., 33%; W.B.C., 4,400/c.mm.; T.P., 5.6 g./100 ml.; A., 1.7 g./100 ml.; marrow Fe, nil; sids., 0%; R.C.P., 10%.

May 20: Hb, 10.4 g./100 ml.; P.C.V., 35%; W.B.C., 8,900/c.mm.; T.P., 6.3 g./100 ml.; A., 2.4 g./100 ml.; marrow Fe, nil; sids., 0%; R.C.P., 12%; G.S.C., for which folic acid was given.

June 4: Hb, 10.2 g./100 ml.; P.C.V., 35%; W.B.C., 9,900/c.mm.; T.P., 7.3 g./100 ml.; A., 2.4 g./100 ml.; marrow Fe, nil; sids., 40%; R.C.P., 17%.

June 21: Hb, 10 g./100 ml.; P.C.V., 35%; W.B.C., 10,000/c.mm.; T.P., 8.3 g./100 ml.; A., 2.6 g./100 ml.; marrow Fe, nil; sids., 0%; R.C.P., 9%. As there was no improvement in the Hb and P.C.V. for nearly a month and the R.C.P. was falling, oral riboflavine 3 mg. daily was given for two weeks.

June 30: Marrow Fe, nil; sids., 8%; R.C.P., 32%.

July 7: Two weeks after the first dose of riboflavine, Hb, 11.6 g./100 ml.; P.C.V., 40%; W.B.C., 12,000/c.mm.; T.P., 8.3 g./100 ml.; A., 3.3 g./100 ml.; left hospital.

Case 3

A 2-year-old Kikuyu boy entered hospital on May 27, 1960, with typical kwashiorkor and a one-week history of cough and diarrhoea. Hb, 8.4 g./100 ml.; P.C.V., 31%; W.B.C., 5,500/c.mm.; T.P., 3.8 g./100 ml.; A., 1.1 g./100 ml.; marrow Fe, lumps grade 4; sids., 78%; R.C.P., 22%.

May 30: Moist sounds in lungs; temperature 100° F. (37.8° C.); penicillin and streptomycin, and as

June 10: Hb, 8.4 of these av P.C.V., 31%; W.B.C., 14,000/c.mm.; T.P. garded as ml.; A., 1.72 g./100 ml.; marrow Fe, nil; sid R.C.P., 37%.

June 23: Child much better clinically, but routine haematological examination showed: Hb, 8.4 g./100 ml.; P.C.V., 31%; W.B.C., 11,000/c.mm.; T.P., 7.3 g./100 ml.; A., 3.3 g./100 ml.; marrow Fe, nil; sids., 0%; R.C.P., 4%. Since the Hb had remained stable for three weeks and the marrow became hypoplastic, oral riboflavine 3 mg. daily was given for two weeks.

July 1: Seven days after the first dose of riboflavine marrow Fe nil; sids., 20%; R.C.P., 31%.

July 8: Hb and P.C.V. went up for the first time since the child entered hospital. Hb, 10.7 g./100 ml.; P.C.V., 40%; T.P., 7.7 g./100 ml.; A., 2.84 g./100 ml.; left hospital.

Case 4

A 1-year-old Kikuyu girl entered hospital on May 27, 1960, with typical marasmus/kwashiorkor and a two-weeks history of diarrhoea; temperature 100° F. (37.8° C.); Hb, 7.8 g./100 ml.; P.C.V., 27%; W.B.C., 6,300/c.mm.; T.P., 3.6 g./100 ml.; A., 1.1 g./100 ml.; marrow Fe, lumps grade 4; sids., 65%; R.C.P., 16%.

June 10: Hb, 4.5 g./100 ml.; P.C.V., 17%; W.B.C., 4,580/c.mm.; T.P., 6.3 g./100 ml.; A., 1.8 g./100 ml.; marrow Fe, grade 4; sids., 0%; R.C.P., 3%. As the patient's Hb, P.C.V., and R.C.P., went down so precipitously she was given a transfusion of 100 ml. of blood and 3 mg. of oral riboflavine for two weeks.

June 17: One week after the first dose of riboflavine marrow Fe, grade 3; sids., 0%; R.C.P., 78%; G.S.C. for which folic acid and vitamin B_{12} were given.

June 24: Hb rose to 8.4 g./100 ml.; P.C.V., 31%; W.B.C., 10,000/c.mm.; T.P., 6.9 g./100 ml.; A., 2.8 g./100 ml.

July 8: Hb, 9.7 g./100 ml.; P.C.V., 34%; W.B.C., 7,000/c.mm.; marrow Fe, grade 2; sids., 0%; R.C.P., 17%.

July 21: Hb, 9.7 g./100 ml.; P.C.V., 34%; W.B.C., 6,600/c.mm.; T.P., 6.8 g./100 ml.; A., 2.7 g./100 ml.; marrow Fe, grade 2; sids., 0%; R.C.P., 2%. As the Hb and P.C.V. stopped rising and the R.C.P. again fell riboflavine 5 mg. daily intramuscularly was given for two weeks.

August 5: Two weeks after the second course of riboflavine, Hb, 10.6 g./100 ml.; P.C.V., 37%; W.B.C., 8,400/c.mm.; T.P., 6.3 g./100 ml.; A., 2.96 g./100 ml.; marrow Fe, grade 2; sids., 0%; R.C.P., 26%. Left hospital.

Case 5

A 4-year-old Mkamba boy entered hospital on July 7, 1960, with typical kwashiorkor and a two-months history of diarrhoea and giardiasis, for which mepacrine was given. Hb, 5.2 g./100 ml.; P.C.V., 17%; W.B.C., 8,500/c.mm.; T.P., 6 g./100 ml.; A., 2.9 g./100 ml.; marrow malaria pigment, no Fe; sids., 60%; R.C.P., 47%.

July 21: Developed measles. Hb, 8.3 g./100 ml.; P.C.V., 34%; W.B.C., 4,800/c.mm.; T.P., 6.8 g./100 ml.; A., 2.64 g./100 ml.; marrow malaria pigment, no Fe; sids., 0%; R.C.P., 16%.

August 8: Recovered from measles. Hb, 9.7 g./100 ml.; P.C.V., 39%; W.B.C., 10,500/c.mm.; T.P., 7.3 g./100 ml.; A., 3.1 g./100 ml.; marrow no malaria pigment, no Fe; sids., 0%; R.C.P., 2%.

August 17: Child much better clinically; but Hb, 8.4 g./100 ml.; P.C.V., 32%; W.B.C., 14,000/c.mm.; T.P., 7.8 g./100 ml.; A., 4 g./100 ml.; marrow Fe, nil; sids., 0%; R.C.P., 1%. As the marrow was found to be aplastic on two occasions, riboflavine 5 mg. daily intramuscularly was given for five weeks.

August 24: One week after the first dose of riboflavine. Marrow Fe, nil; sids., 0%; R.C.P., 28%.

August 30: Hb, 9.3 g./100 ml.; P.C.V., 31%.

September 9: Hb, 9.9 g./100 ml.; P.C.V., 37%.

September 15: Hb, 9.9 g./100 ml.; P.C.V., 37%; marrow, no malaria pigment, no Fe; sids., 0%; R.C.P., 19%; heavy giardia infection, mepacrine given.

September 26: Hb, 11 g./100 ml.; P.C.V., 41%. The slow haematological response of this child was probably

due to repeated occurrences of giardia infection, and once these were effectively treated the haemoglobin rose to normal.

September 28: Left hospital.

Discussion

Our attention was first drawn to this red-cell aplasia of the marrow in a patient from whom two successive marrow specimens taken from the spinous processes yielded what appeared to be blood; a third puncture, from the tibia, produced a similar fluid, which, however, on examination was found to contain marrow particles, proving upon scrutiny to be completely devoid of all R.C.P.s.

The aetiological factors concerned in the present cases of selective red-cell aplasia are obscure. Gross malnutrition and diarrhoea were present in all the 23 cases of marasmus and kwashiorkor, and most had respiratory as well as other infectious processes, but only nine of them developed aplasia or hypoplasia, for which it was impossible to decide what particular factors were responsible.

In none of the present cases was there obvious clinical or radiological thymic enlargement, or history of exposure to toxic substances or ionizing radiations. Indirect bilirubin was never raised and there was no sign of haemolysis. Some of the patients had been given mepacrine (an antagonist of riboflavine) for giardia infection, but others had not. One had miliary tuberculosis, and one had malaria pigment in the marrow, but we know of no evidence to incriminate these as causes of pure red-cell aplasias. That tetracycline or penicillin and streptomycin, which are currently used in the treatment of marasmus and kwashiorkor, were in any way involved in the causation of these aplasias seems unlikely. So far as we are aware, there is little evidence that these antibiotics produce depression of the red-cell series in the bone-marrow. In fact, there was no common denominator that could be specifically incriminated as a cause of the aplasias.

On admission the bone-marrow was always erythronormoblastic and sometimes had considerable numbers of R.C.P.s (Table I); two patients had G.S.C.s. In all cases hypoplasia or aplasia developed during treatment at a time when the serum proteins were returning to normal (Table I). At the stage when the marrow was aplastic or hypoplastic in the red-cell series, the myeloid series and platelets were normal in all the patients and there was no sign of panmyelopathy, the only series affected being the erythroid. In Table II are shown the myeloid series at a time when the marrow was hypoplastic or aplastic in the red-cell line.

In some cases there was an increase in the reticulum cells. Every case showed an increase in the lymphocytes such as was described by Chalmers and Boheimer (1954). Perhaps some of these lymphocytes were the "erythrogones" of Israëls (1948) and may be precursors of the red cells. Alternatively, the factors responsible for the aplasia may also be causing the lymphocytosis, in which case there is no need to suppose that these lymphocytes are taking any part in red-cell production.

From admission till the development of aplasia there were great fluctuations in the cellularity of the marrow, but ultimately the R.C.P.s fell to less than 5% in all patients but one (Case 2).

The development of this aplasia during the course of treatment is interesting in view of the findings of Gómez *et al.* (1952, 1955), who described a "recovery

TABLE I

Date	Hb g./100 ml.	P.C.V. %	M.C.H.C. %	R.C.P. %	E.E. %	L.E. %	N. %	Sids. %	Marrow Iron Grade	Retics. %	T.P. g./100 ml.	A. g./100 ml.
Case 1												
30/4/60	9·5	33	29	17	3	5	9	70	4	—	3·0	1·04
20/5/60	8·5	31	28	38	2	15	21	0	2	—	5·5	2·04
11/6/60	9·4	35	27	11	1	3	7	0	1	—	6·5	2·2
24/6/60	9·4	35	27	32	9	4	19	0	1	—	6·8	3·5
11/7/60	9·4	35	27	0	0	0	0	0	1	0	6·7	3·1
18/7/60	8·0	—	—	0	0	0	0	0	1	0	—	—
Riboflavine												
25/7/60	—	—	—	—	—	—	—	—	—	1		
26/7/60	—	—	—	—	—	—	—	—	—	2		
27/7/60	—	—	—	—	—	—	—	—	—	4		
28/7/60	—	—	—	—	—	—	—	—	—	9		
29/7/60	—	—	—	—	—	—	—	—	—	7		
30/7/60	—	—	—	—	—	—	—	—	—	6		
2/8/60	8·8	33	27	25	3	5	17	4	0	3	6·8	3·1
9/8/60	9·6	36	27	—	—	—	—	—	—	—	—	—
16/8/60	10·5	38	28	17	5	6	6	29	0	3	7·8	3·5
29/8/60	11·7	43	27	—	—	—	—	—	—	—	—	—
Case 2												
30/3/60	9·4	33	28	10	2	2	6	0	0	—	5·6	1·7
20/5/60	10·4	35	30	12	3	1	8	0	0	—	6·3	2·4
4/6/60	10·2	35	29	17	0	2	15	40	0	—	7·3	2·4
21/6/60	10·0	35	29	9	3	2	4	0	0	—	8·3	2·6
Riboflavine												
30/6/60	—	—	—	32	3	12	17	8	0	—	—	—
7/760	11·6	40	29	—	—	—	—	—	—	—	8·3	3·3
Case 3												
27/5/60	8·4	31	27	22	6	7	9	78	4	—	3·8	1·1
10/6/60	8·4	31	27	37	2	17	18	10	0	—	6·4	1·7
23/6/60	8·4	31	27	4	3	1	0	0	0	—	7·3	3·3
Riboflavine												
1/7/60	—	—	—	31	3	10	18	20	0	7	—	—
8/7/60	10·7	40	27	—	—	—	—	—	—	—	7·7	2·8
Case 4												
27/5/60	7·8	27	29	16	1	5	10	65	4	—	3·6	1·1
10/6/60	4·5	17	26	3	2	0	1	0	4	—	6·3	1·8
Riboflavine												
17/6/60	—	—	—	78	10	49	19	0	3	—	—	—
24/6/60	8·4	31	27	—	—	—	—	—	—	—	6·9	2·8
8/7/60	9·7	34	28	17	1	3	13	0	2	—	—	—
21/7/60	9·7	34	28	2	0	1	1	0	2	—	6·8	2·7
Riboflavine												
5/8/60	10·6	37	29	26	3	6	17	0	2	—	6·3	3·0
Case 5												
7/7/60	5·2	17	30	47	3	20	24	60	M.P.	—	6·0	2·9
21/7/60	8·3	34	24	16	4	1	11	0	M.P.	—	6·8	2·6
8/8/60	9·7	39	25	2	1	1	0	0	No M.P.	0	7·3	3·1
17/8/60	8·4	32	26	1	1	0	0	0		0	7·8	4·0
Riboflavine												
24/8/60	—	—	—	28	6	10	12	0	0	3		
25/8/60	—	—	—	—	—	—	—	—	—	8		
26/8/60	—	—	—	—	—	—	—	—	—	6		
27/8/60	—	—	—	—	—	—	—	—	—	4		
30/8/60	9·3	36	25	—	—	—	—	—	—	2		
9/9/60	9·9	37	27	—	—	—	—	—	—	—		
15/9/60	9·9	37	27	19	1	8	10	0	0	—		
26/9/60	11·0	41	27	—	—	—	—	—	—	—		

Hb = Haemoglobin. P.C.V. = Packed cell volume. M.C.H.C. = Mean corpuscular haemoglobin concentration. R.C.P. = Red-cell precursors. E.E. = Early erythroblasts. L.E. = Late erythroblasts. N. = Normoblasts. Sids. = Sideroblasts. Retics. = Reticulocytes. T.P. = Total protein. A. = Albumin.

TABLE II.—*Differential Marrow Counts at Time of Red-cell Aplasia*

	Case 1		Case 2	Case 3	Case 4		Case 5	
	11/7	18/7	21/6	23/6	10/6	21/7	8/8	17/8
Myeloblasts, % ..	3	0	0	0	0	3	2	0
Promyelocytes, %	1	2	1	2	3	1	0	1
Myelocytes, % ..	7	8	13	5	12	3	4	3
Metamyelocytes, %	11	10	9	2	3	2	3	2
Polymorphs, % ..	45	34	40	32	25	18	46	32
Lymphocytes, %	26	41	23	48	37	45	37	53
Eosinophils, %	3	4	2	7	1	4	2	3
Basophils, %	0	0	0	0	2	0	1	0
Reticulum cells, % ..	2	0	2	0	6	14	2	5
Megakaryocytes, %	1	0	0	0	0	0	0	0
Monocytes, %	1	0	0	0	4	6	1	0
Plasma cells, % ..	0	1	1	0	4	2	0	0
W.B.C. ..	6,600	—	10,000	11,000	4,580	6,600	10,500	14,000

syndrome" in malnutrition developing two to three weeks after the beginning of treatment and involving hepatomegaly, ascites, eosinophilia, and perhaps associated with "dysadrenocorticism" (Iversen, 1955), in which riboflavine deficiency plays a part (Forker and Morgan, 1954, 1955; Slater, 1959; *Nutrition Reviews*, 1960). Perhaps this red-cell aplasia is another manifestation of the "recovery syndrome." The aplasia and the other symptoms of the "recovery syndrome" may be due to deficiency of cortisone which is itself linked to riboflavine deficiency.

We do not know what proportion of cases of red-cell aplasia occurring in marasmus and kwashiorkor recover spontaneously without riboflavine, or how many deaths are due to bone-marrow failure. Spontaneous recovery, although not unknown, is exceedingly rare (Heilmeyer and Begemann, 1951). It is possible that the aplasia may be symptomatic and self-limiting; in two cases, however, an aplastic marrow was found in patients who had left hospital and who later died. Whatever the ultimate prognosis of these aplasias, they appear to be a common accompaniment of marasmus and kwashiorkor in Kenya, and must be regarded as a serious complication.

As in the previous case of pure red-cell aplasia reported in an African (Foy and Kondi, 1953), the response to riboflavine in the present patients was clear-cut. So far as was consistent with the clinical and haematological condition, riboflavine administration was begun only when the R.C.P.s had fallen to 5% or less, and was continued for from two to six weeks either orally or intramuscularly. One week after the first dose of riboflavine the bone-marrow passed from a state of hypoplasia or complete red-cell aplasia to a condition in which 25%–78% of the cells were R.C.P.s, consisting of early and late erythroblasts and normoblasts, and followed by peripheral reticulocytosis. One week after this increase in marrow activity there was a rise in the Hb and P.C.V. The time-relation between the administration of riboflavine and the subsequent haematological response makes it appear that there was an association between the two. Further, in Case 4 an increase in marrow activity followed the administration of riboflavine, but when this was stopped the cellularity of the marrow decreased, becoming reactivated when riboflavine was resumed; this second response must, we think, be regarded as significant. As was to be expected the increase in R.C.P.s after riboflavine was more pronounced in the most anaemic cases.

Altman and Miller (1953) reported an increased excretion of anthranilic acid in the urine of a patient with pure red-cell aplasia; after treatment with riboflavine the urinary anthranilic acid disappeared but the aplasia was unaffected. Altman and Miller attributed the presence of anthranilic acid to upsets in tryptophan metabolism due to a deficiency of riboflavine. Mason (1953) has shown that when tryptophan is administered to riboflavine-deficient rats there is a considerable increase in the output of anthranilic acid. These reports indicate that riboflavine is in some way linked with tryptophan metabolism. We had no facilities at the time for chromatographic studies, and we cannot at present say whether the patients had abnormal outputs of urinary anthranilic acid; serum riboflavine was not estimated in the present cases.

Whatever the cause of the pure red-cell aplasia in the patients under consideration, it seems that it is favourably influenced by riboflavine. According to Scrimshaw *et al.* (1956), serum riboflavine is often very low in kwashiorkor, and rises during treatment because of the milk diet. In the present patients, in spite of the milk diet, the serum riboflavine may have failed to increase enough to stimulate and sustain marrow activity, or their demands for riboflavine were greater than in those who did not become aplastic. The low level of serum riboflavine that occurs in these conditions may be due to the malnutrition, the diarrhoea, or the infections, and may apply to other vitamins as well (Scrimshaw *et al.*, 1956).

It is possible also that the high-protein diet which is an essential part of the treatment of these conditions increases the demand for riboflavine, leaving insufficient for sustaining increased marrow activity, just as excessive protein in the diet has been found to increase demands for vitamin B_{12} in both megaloblastic and iron-deficient anaemias (Foy and Kondi, 1958; Foy, Kondi, and Sarma, 1958).

Haemosiderin was present in the marrow as lumps in three cases, and this is usually regarded as an indication of some infectious process (Rath and Finch, 1948; Heilmeyer and Wöhler, 1958; Wallerstein and Pollycove, 1958; Heilmeyer and Keiderling, 1959). It may, however, have been associated with the very low serum proteins and a consequent reduction in transferrin leading to precipitation of the absorbed iron as haemosiderin (Shoden and Sturgeon, 1959). This shift of the iron from the red cells to the storage depots, resulting in an increase in marrow haemosiderin, is common in many anaemias, and the marrow iron in such cases decreases with treatment (Sheehy *et al.*, 1960). One of the patients, although miliary tuberculosis was present, had no haemosiderin in the marrow; this may have been because the iron stores were excessively low. Another had masses of malaria pigment in the marrow, and it is our experience that when iron is present in the marrow in the form of malaria pigment iron in other forms cannot be found.

With the exception of the tuberculosis patient, all the others had high sideroblast levels on admission to hospital, and these fluctuated widely throughout their illness.

In spite of the presence of haemosiderin and sideroblasts in the marrow on admission, the anaemia was always hypochromic, as it is in chronic infection (Heilmeyer and Begemann, 1951). During the course of the illness marrow iron and sideroblasts fell or disappeared, but iron therapy was necessary to meet the demands of increased marrow activity and to sustain haemopoiesis.

The serum iron was low on admission and fluctuated in relation to variations in haemopoiesis. The unsaturated iron-binding capacities and iron-saturation indices paralleled the fluctuations in serum iron and protein variations. The changes in these variables form a very striking picture in marasmus and kwashiorkor, and will be dealt with in a later paper.

Whatever factors are involved in the high incidence of pure red-cell aplasia in marasmus and kwashiorkor, it seems that riboflavine is playing an important part in haemopoiesis, and is one of the substances that take part in some enzyme system that potentiates the maturation of a primitive stem cell into erythroblasts acting either directly or through the steroid hormones.

Summary

Selective red-cell aplasia or hypoplasia occurred in 9 out of 23 cases of marasmus and kwashiorkor in Kenya.

Serial bone-marrow punctures showed that the red-cell precursors were normal on admission, and the marrow became hypoplastic or completely aplastic during recovery, at a time when the serum proteins were returning to normal.

There was no single factor that could be regarded as a cause of these red-cell aplasias.

Treatment with oral or intramuscular riboflavine reactivated the marrow and was followed by reticulocytosis and a rise in haemoglobin and packed cell volume.

The implications of the marrow aplasia in marasmus and kwashiorkor are discussed.

Both the adrenal dysfunction of the "recovery syndrome" and the red-cell aplasia may be associated with riboflavine deficiency, particularly as the serum riboflavine is low in marasmus and kwashiorkor and the aplasia responds to riboflavine.

Our thanks are due to the Kenya Medical Department and the medical and nursing staff of the children's ward of the King George VI Hospital for help and assistance given to us during these investigations.

REFERENCES

Altman, K. I., and Miller, G. (1953). *Nature (Lond.)*, **172**, 868.
Chalmers, J. N. M., and Boheimer, K. (1954). *Brit. med. J.*, **2**, 1514.
Dean, R. F. A., and Schwartz, R. (1953). *Brit. J. Nutr.*, **7**, 131.
Forker, B. R., and Morgan, A. F. (1954). *J. biol. Chem.*, **209**, 303.
—— —— (1955) Ibid., **217**, 659.
Foy, H., and Kondi, A. (1953). *J. Path. Bact.*, **65**, 559.
—— —— (1958). *Trans. roy. Soc. trop. Med. Hyg.*, **52**, 46.
—— —— and Sarma, B. (1958). *J. trop. Med. Hyg.*, **61**, 27.
Freeman, Z. (1960). *Brit. med. J.*, **1**, 1390.
Gómez, F., Ramos Galván, R., and Cravioto Muñoz, J. (1952). *Pediatrics*, **10**, 513.
—— —— Cravioto, J., and Frenk, S (1955). *Advanc. Pediat.*, **7**, 131.
Gornall, A. G., Bardawill, C. J., and David, M. M. (1949). *J. biol. Chem.*, **177**, 751.
Heilmeyer, L., and Begemann, H. (1951). *Blut und Blutkrankheiten*. Springer, Berlin.
—— and Keiderling, W. (1959). *Dtsch. med. Wschr.*, **84**, 724.
—— and Wöhler, F. (1958). *Dtsch. med. Wschr.*, **83**, 1965.
Israëls, M. C. G. (1948). *Atlas of Bone Marrow Pathology*. Heinemann, London
Iversen, T. (1955). *Pediatrics*, **16**, 875.
Jacobs, E. M., Hutter, R. V., Pool, G. L., and Ley, A. B. (1959). *Cancer*, **12**, 47.
Jelliffe, D. B., and Dean, R. F. A. (1959). *J. trop. Pediat.*, **5**, 96.
Mason, M. (1953) *J. biol. Chem.*, **201**, 513.
Nutr. Rev., 1960, **18**, 180.
Rath, C. E., and Finch, C. A (1948). *J. Lab. clin. Med.*, **33**, 81.
Scrimshaw, N. S., Behar, M., Arroyave, G., Viteri, F., and Tejadá, C. (1956). *Fed. Proc.*, **15**, 977.
—— —— —— —— (1957). *Amer. J. publ. Hlth*, **47**, 53.
Sheehy, T., Rubini, M. E., Baco-Dapena, R., and Perez-Santiago, E. (1960). *Blood* **15**, 761.
Shoden, A., and Sturgeon, P. H. (1959). *Acta haemat. (Basel)*, **22**, 140.
Slater, G. G. (1959). *Endocrinology*, **65**, 731.
Wallerstein, R. O., and Pollycove, M. (1958). *Arch. intern. Med.*,

A Government White Paper, *Disabled Persons in Government Employment*, shows that the Government employ 41,744 registered disabled persons. In the non-industrial Civil Service there are 627,127 people employed, of whom 26,554 (4.2%) are disabled. In the industrial Civil Service there are 349,711 people employed and 14,768 of them are disabled, again 4.2%. There are 452 passenger-lift attendants and 422 of them are disabled, or 93.4%. The standard percentage for the purpose of the Disabled Persons (Standard Percentage) Order, 1946, is 3%.

PRIMAQUINE-SENSITIVITY OF RED CELLS IN VARIOUS RACES IN SOUTHERN AFRICA

BY

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AND

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Some cases of drug-induced haemolytic anaemia have been shown to be due to the action of the drug on congenitally defective red blood cells (Beutler, 1959). Phenacetin, acetanilide, sulphanilamide, sulfoxone, thiazosulphone (Dern *et al.*, 1955), nitrofurantoin (Kimbro *et al.*, 1957), pamaquin, and primaquine (Dern *et al.*, 1955) belong to this group. In addition, favus beans (Sansone and Segni, 1957) and naphthalene (Zinkham and Childs, 1957) also cause haemolysis in sensitive individuals. The congenitally defective red cell has a normal life span unless exposed to one of the precipitating substances, and the trait has not been shown to lead to any other disability. Since the biochemical lesion was first characterized in subjects sensitive to the antimalarial primaquine the condition is commonly referred to as "primaquine sensitivity."

Red-cell Abnormalities in Susceptible Subjects

The pattern of haemolysis in susceptible subjects exposed to one of the precipitating agents has certain characteristic features (Dern *et al.*, 1954; Flanagan *et al.*, 1958). It begins on about the third or fourth day of administration and lasts until about the twelfth day. About half the red-cell population is destroyed, with the result that the haemoglobin and haematocrit fall to roughly half their original values. Haemolysis then ceases, and the blood picture rapidly returns to normal. This is true even when the patient continues to take the drug. The clinical picture is thus one of an acute self-limited haemolytic anaemia.

The defective red cells can be identified in several ways. The first distinguishing characteristic to be discovered was abnormal Heinz-body formation *in vitro*. Following on the clinical observation that Heinz bodies appeared transitorily in the red cells of sensitive volunteers taking primaquine (Beutler *et al.*, 1954), it was demonstrated *in vitro* that the Heinz bodies produced in sensitive cells differed from those in normal cells both in size and in number (Beutler *et al.*, 1955), and the Heinz-body test has been used as a method of predicting primaquine sensitivity.

Subsequent investigations have revealed several biochemical abnormalities in the red cells of susceptible subjects. The concentration of reduced glutathione tends to be lower than normal, though the difference is not great enough to be used as a test of sensitivity. Of more significance is the fact that the glutathione level drops sharply on incubation *in vitro* with acetylphenylhydrazine, while the level in normal blood does not change. This glutathione stability test has proved an accurate means of predicting primaquine sensitivity (Beutler, 1957).

*In receipt of a grant from the Council for Scientific and Industrial Research, South Africa.

More recently several enzymatic abnormalities have been demonstrated in sensitive cells. The enzyme glucose-6-phosphate dehydrogenase has been shown to be present in quantities much below normal levels (Carson *et al.*, 1956). This enzyme catalyses the first step in the direct oxidation of glucose via the hexose-monophosphate shunt. In this reaction glucose-6-phosphate is oxidized to 6-phospho-gluconate, and the hydrogen which is removed reduces coenzyme II (triphosphopyridine nucleotide). Coenzyme II is reoxidized by glutathione, which in turn is reduced in the process (Schrier *et al.*, 1958). Glucose-6-phosphate dehydrogenase activity may be estimated in red cells, and deficiency implies primaquine sensitivity. Sensitive cells have also been shown to have increased glutathione reductase (Schrier *et al.*, 1958) and aldolase (Schrier and Kellermeyer, 1958) activity. These abnormalities are regarded at the present time as compensatory to the primary deficiency of glucose-6-phosphate dehydrogenase, the first by facilitating reduction of oxidized glutathione and the second by increasing the maximum rate of anaerobic glycolysis (Schrier and Kellermeyer, 1958). It is, however, still not clear why certain chemical agents should cause haemolysis of red cells with these various biochemical abnormalities (Beutler, 1959).

The condition is hereditary, and although further study is necessary, it appears to be transmitted by a sex-linked incompletely dominant gene (Childs *et al.*, 1958). Thus, males and homozygous females have unstable glutathione and low levels of glucose-6-phosphate dehydrogenase, while female heterozygotes show all degrees of glutathione instability and glucose-6-phosphate dehydrogenase activity. Racial distribution of the trait varies considerably. It is rare in white Americans but is found in 7 to 14% of American negroes (Beutler, 1957; Childs *et al.*, 1958). About 11% of Sephardic Jews have the trait, while it occurs rarely, if at all, in Ashkenazic Jews (Szeinberg *et al.*, 1958). It is relatively common in Greeks and Italians (Gross *et al.*, 1958; Childs *et al.*, 1958), but uncommon in Chinese (Beutler *et al.*, 1959).

Since there is no information on the incidence of the trait in Southern Africa, a survey was carried out in which blood from Bantu, Indians, Cape Malays, and Kalahari Bushmen was examined.

The Investigation

Of the 310 Bantu males tested, 129 were patients in hospital suffering from a variety of medical and surgical conditions, while 181 were healthy blood donors. The 53 Cape Malays tested were male patients in Groote Schuur Hospital, Capetown, and the 100 Indian males were patients in King Edward VII Hospital, Durban. Specimens of Bushman blood were obtained from 29 males and 41 females: 16 males and 31 females belonged to the Central Kalahari Bushman group; while 13 males and 10 females were of the Northern group. These specimens were refrigerated and flown to Johannesburg shortly after collection.

Methods

The glutathione stability test was performed by the method of Beutler (1957) as modified by Flanagan *et al.* (1958). The Heinz-body test was carried out as described by Beutler *et al.* (1955). Glucose-6-phosphate dehydrogenase activity was estimated by the screening method of Motulsky and Campbell (1961), which depends upon the decolorization of a fixed amount of the dye brilliant cresyl blue within a certain time. Glucose-6-phosphate and coenzyme II are added to the haemolysate, and the speed of the reaction thus depends on the quantity of enzyme present. The method has proved reliable and well suited to population survey studies.

Initially heparinized venous blood was used, but the necessity of performing the test within three hours of collection was a disadvantage, and in most studies the blood was collected in acid-citrate-dextrose solution. This permits a delay of at least some days before testing (Beutler, 1959). In a number of studies in which the test for glucose-6-phosphate dehydrogenase activity was used as the screening procedure the blood was obtained by digital puncture.

In all cases positive results were confirmed by applying a second test. At the beginning of the investigation glutathione stability tests were done on all specimens and glucose-6-phosphate dehydrogenase activity or the Heinz-body test was carried out on those with unstable glutathione. In later studies the screening test for glucose-6-phosphate dehydrogenase activity was used as the initial procedure and the glutathione stability test was performed on those with diminished enzyme activity.

Validation of Techniques.—In order to test the validity of the techniques employed two approaches were used. In the first, blood from a subject who had previously been reported as suffering from favism (Senior and Braudo, 1955) was tested. The cells were shown to form typical abnormal Heinz bodies and the concentration of reduced glutathione fell from a basal level of 51 mg./100 ml. erythrocytes to 10.6 mg./100 ml. on incubation with acetylphenylhydrazine. In addition, the screening test for glucose-6-phosphate dehydrogenase showed a marked decrease in enzyme activity. In the second test, red cells from an individual regarded as positive on the three screening tests were labelled with Cr-51 as described by Mollison and Veall (1955) and injected into the circulation of a normal compatible recipient. For eight days the rate of disappearance of radioactivity from the blood of the recipient was compatible with a normal survival of the deficient donor cells. Primaquine was then administered in a dosage of 30 mg. daily. On the third day a sharp increase in rate of disappearance of radioactivity was observed (Fig. 1), thus indicating that the cells were, in fact, sensitive to primaquine.

Results

Bantu.—In 182 Bantu males glutathione stability tests were performed as the initial test. The test was regarded as positive in five. In these subjects the average concentration of reduced glutathione after incubation with acetylphenylhydrazine was 12.3 mg./100 ml. red cells (range 8.2–18 mg./100 ml.). In the 177 negative reactors the average concentration after incubation was 54.4 mg./100 ml. (range 31–156.8 mg./100 ml.). In the five subjects with unstable glutathione the Heinz-body test was found to be positive. In a further 128 Bantu males blood samples were examined for glucose-6-phosphate dehydrogenase activity and five were found to be deficient. Glutathione stability tests were positive in each of these subjects with post-incubation values

ranging between 1 and 11 mg./100 ml. red cells. (The results of the initial 182 glutathione stability tests and of the additional five positive ones are shown in Fig. 2 and the tribal origins of all the subjects tested are shown in the Table.)

Tribal Origins of the Bantu Males Studied

Tribe	No. Tested	No. Positive
Msutu	74	2
Zulu	73	1
Xhosa	43	1
Tswana	25	2
Shangaan	18	1
Pedi	11	0
Swazi	8	1
Nyasa	7	1
Coloured (mixed origins)	13	1
Remainder (Baca, Pondo, Venda, etc.)	38	0
Total	310	10

Indians.—Blood obtained by digital puncture from 100 Indian males was tested for glucose-6-phosphate dehydrogenase activity. In no case was deficiency of the enzyme demonstrated.

Cape Malays.—The blood from 53 male Cape Malays was tested for glucose-6-phosphate dehydrogenase activity. Two specimens were deficient in the enzyme. The reduced glutathione concentrations of these bloods after incubation with acetylphenylhydrazine were 7.4 and 4.5 mg./100 ml. red cells respectively.

Bushmen.—Blood samples from 29 males and 41 females were tested for glucose-6-phosphate dehydrogenase activity. Two samples, one from a male and one from a female, were found to be deficient in the enzyme. The concentrations of reduced glutathione after incubation in these two cases were 0 and 10 mg./100 ml. red cells respectively. Both positive reactors were of the Central Kalahari group.

Comment

The results of the present investigation suggest that the incidence of primaquine sensitivity of the red cells in the Bantu of Southern Africa is approximately 3%. The 10 positive reactors detected belonged to a number of different tribes, as shown in the Table, but the numbers are not large enough for the tribal incidences to be determined. The finding of the trait in the Bantu is not surprising as pamaquin haemolysis has previously been noted in a Nyasa soldier (Mann, 1943) and in a Basuto (Smith, 1943). The incidence is, however, a good deal lower than has been reported in the majority of East African tribes, where it appears to parallel that of the sickle trait (Allison, 1960).

Although the defect was also found to be present in Cape Malays and Bushmen, the significance of the findings in the Malays is open to question, as they are not a pure racial group but represent crossbred descendants of Asiatics, Bantu, Hottentots, Bushmen, and Europeans (du Plessis, 1944).

Although none of the Indians tested showed evidence of glucose-6-phosphate dehydrogenase deficiency, it is evident that the trait does occur in India, as there are several reports of haemolysis due to pamaquin in Indian subjects (Manifold, 1931; Amy, 1934; Sein, 1937; Proc. Conf. Med. Spec., 1944; Dimson and McMartin, 1946). However, most of these patients were Northern Indians, while the Indians of Natal are for the most part descendants of immigrants from Madras (Shafa'at Ahmad Khan, 1946). It is thus possible that the gene frequency varies in different parts of India.

Summary

Red blood cells genetically deficient in glucose-6-phosphate dehydrogenase and with unstable glutathione haemolyse when exposed to certain drugs, chemicals, and favus beans.

The trait has been demonstrated in approximately 3% of Bantu males and has also been found to be present in Cape Malays and Bushmen. It has not been observed in 100 Indian males from Natal.

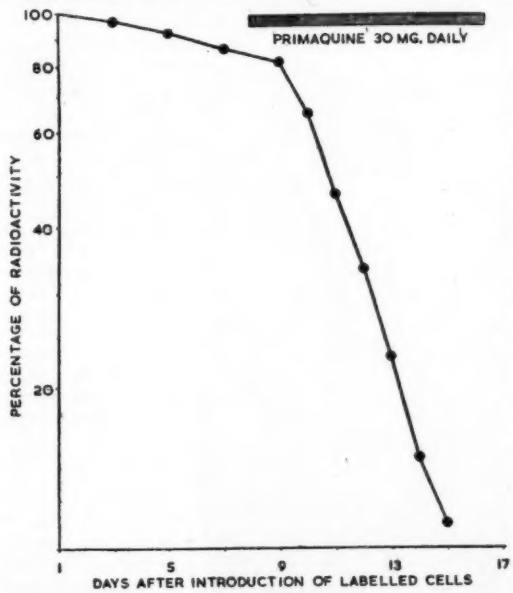

FIG. 1

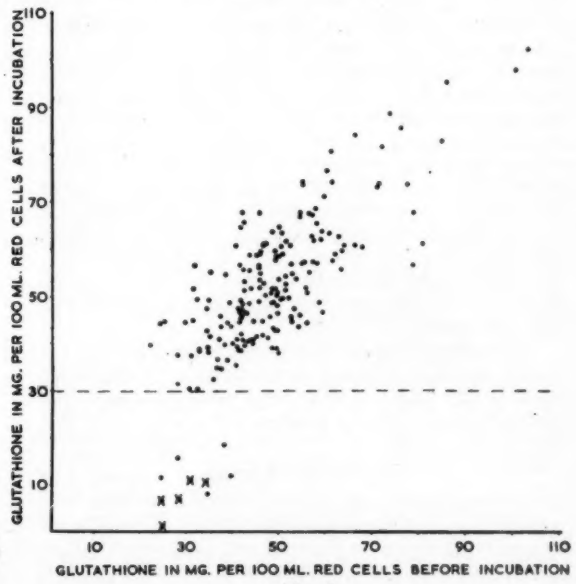

FIG. 2

FIG. 1.—Rate of disappearance of radioactivity from blood before and during administration of primaquine. FIG. 2.—Results of glutathione stability tests.

REFERENCES

Allison, A. C. (1960). *Nature (Lond.)*, **186**, 531.
Amy, A. C. (1934). *J. roy. Army med. Cps*, **62**, 178.
Beutler, E. (1957). *J. Lab. clin. Med.*, **49**, 84.
—— (1959). *Blood*, **14**, 103.
—— Dern, R. J., and Alving, A. S. (1954). *J. Lab. clin. Med.*, **44**, 177.
—— —— —— (1955). Ibid., **45**, 40.
—— Yeh, M. K. Y., and Necheles, T. (1959). *Nature (Lond.)*, **183**, 684.
Carson, P. E., Flanagan, C. L., Ickes, C. E., and Alving, A. S. (1956). *Science*, **124**, 484.
Childs, B., Zinkham, W. H., Browne, E. A., Kimbro, E. L., and Torbert, J. V. (1958). *Bull. Johns Hopk. Hosp.*, **102**, 21.
Dern, R. J., Beutler, E., and Alving, A. S. (1954). *J. Lab. clin. Med.*, **44**, 171.
—— —— —— (1955). Ibid., **45**, 30.
Dimson, S. B., and McMartin, R. B. (1946). *Quart. J. Med.*, **15**, 25.
du Plessis, I. D. (1944). *The Cape Malays*. Maskew Miller, Capetown.
Flanagan, C. L., Schrier, S. L., Carson, P. E., and Alving, A. S. (1958). *J. Lab. clin. Med.*, **51**, 600.
Gross, R. T., Hurwitz, R. E., and Marks, P. A. (1958). *J. clin. Invest.*, **37**, 1176.
Kimbro, E. L., Sachs, M. V., and Torbert, J. V. (1957). *Bull. Johns Hopk. Hosp.*, **101**, 245.
Manifold, J. A. (1931). *J. roy. Army med. Cps*, **56**, 321.
Mann, W. N. (1943). *Trans. roy. Soc. trop. Med. Hyg.*, **37**, 151.
Molhson, P. L., and Veall, N. (1955). *Brit. J. Haemat.*, **1**, 62.
Motulsky, A. G., and Campbell, J. M. (1961). *Blood*. In press.
Proceedings of the Conference of Medical Specialists, Lahore (1944). *Trop. Dis. Bull.*, **42**, 406.
Sansone, G., and Segni, G. (1957). *Lancet*, **2**, 295.
Schrier, S. L., and Kellermeyer, R. W. (1958). *J. clin. Invest.*, **37**, 928.
—— —— Carson, P. E., Ickes, C. E., and Alving, A. S. (1958). *J. Lab. clin. Med.*, **52**, 109.
Sein, M. (1937). *Indian med. Gaz.*, **72**, 86.
Senior, B., and Braudo, J. L. (1955). *S. Afr. med. J.*, **29**, 1264.
Shafa'at Ahmad Khan (1946). *The Indian in South Africa*. Kitabistan, Allahabad.
Smith, S. (1943). *Trans. roy. Soc. trop. Med. Hyg.*, **37**, 155.
Szeinberg, A., Sheba, C., and Adam, A. (1958). *Blood*, **13**, 1043.
Zinkham, W. H., and Childs, B. (1957). *J. clin. Invest.*, **36**, 938.

COMPLICATIONS OF CHICKEN-POX

BY

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Varicella is a highly infectious disease of children, usually mild in nature, without complications or sequelae. Occasionally, however, the virus of varicella may give rise to a number of complications of varying severity which may occur singly or in association, affecting (in descending order of frequency) the respiratory system, the nervous system, the urinary system, and the skin. Cases of visceral chicken-pox have been reported by Johnson (1940), Nicolaides (1957), and McLachlan (1957). Haemorrhagic chicken-pox is usually associated with other complications and is of grave prognosis; two such cases were seen at the Leicester Isolation Hospital; another had been described by Cohen and Bansmer (1947).

Mostly single cases or complications affecting one system only are described in the literature. This paper describes all the complications of varicella seen in this hospital over a ten-year period.

Survey of Material

Twelve patients with complications of varicella were admitted to this hospital during 1950–9. The hospital admits infectious cases from an area including Leicester City and County, and Rutland, with a total population of about 1,000,000.

*Present address: EMMS Hospital, Nazareth, Israel.

Table I shows the distribution of cases by age and sex, and the fatalities that occurred.

Table II shows the various complications encountered in order of descending frequency. No cases of nephritis or nephrosis were seen. Five patients had symptomless albuminuria and mild pyuria for a short time.

TABLE I

No. of Cases	Age Groups	Sex		Fatalities	
		M	F	M	F
5	1–10	2	3	1	1
1	11–20	1			
2	31–40	2		1	
2	41–50	2			
2	61–85	1	1		
Total 12		8	4	2	1

TABLE II

Complications	No. of Cases		Total	Fatal	Remarks
	M	F			
Disseminated pneumonia	4	2	6	—	Two cases associated with profuse rash, 1 with zoster, 1 with varicella gangrenosa, 1 with meningo-encephalitis, 1 with haemorrhagic varicella and visceral lesions
Encephalitic symptoms	3	2	5	1	Fatal case had haemorrhagic chicken-pox
Albuminuria and leucocytes in urine	4	1	5	—	None had any symptoms referable to genito-urinary system. All urine abnormalities cleared spontaneously
Localized skin complications	2	1	3	—	One had varicella gangrenosa. Two had superinfection with *Staph. aureus*. All were mild
Herpes zoster ..	1	1	2	—	One had superinfection with *Staph. aureus* and pulmonary infarcts. The other had disseminated pneumonia
Pulmonary infarcts	2	—	2	1	Fatal case had thrombosis of pelvic veins
Visceral lesions	—	1	1	1	Varicella haemorrhagica

Pulmonary Complications

Pulmonary complications were the most common. Four of the six cases of disseminated pneumonia were admitted for other complications. None had any symptoms referable to the chest and the diagnosis was made radiologically. The case reports of the other two cases are given below.

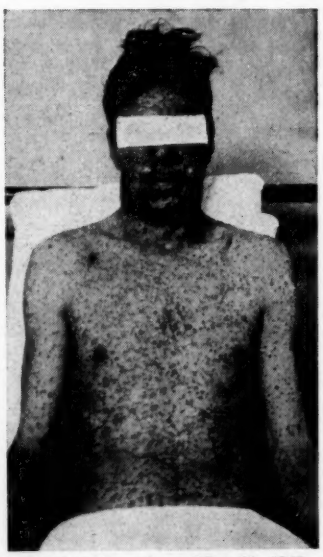

FIG. 1.—Case 3 on May 21, 1950.

Case 3. — Man aged 44; probable source of infection—own child with uncomplicated varicella two weeks prior to illness. May 14, 1950: onset with malaise. May 15: first spots, with rapid increase in spread and density. May 16: upper abdominal pain aggravated by deep breathing; no vomiting, but loss of appetite, normal stools. May 20: admission to hospital. On examination—profuse rash

(Fig. 1), ulcers on gums, palate, and uvula. The rash involved the axillae; there was no adenitis and each lesion was characteristic of chicken-pox. Pain was that of diaphragmatic pleurisy though cough was not marked. There were a few rales in the chest. May 22: rash pustular. May 23: patient lethargic. May 24: scabbing of skin lesions. May 25: patient well enough to be *x*-rayed; widespread disseminated pneumonia (Fig. 2). May 30: thrombosis in right calf, anticoagulant therapy (heparin) started. May 31: pleuritic pain in right chest, pleural friction rub audible; pulmonary infarction diagnosed. June 10: clearing of lesions but thickening of right pleura evident. June 12: discharged. August 10: Follow-up, *x*-ray film clear except for increased bronchovascular markings. Symptom-free. Albuminuria + to ++, and leucocytes were found on several occasions. Total duration of illness was 30 days.

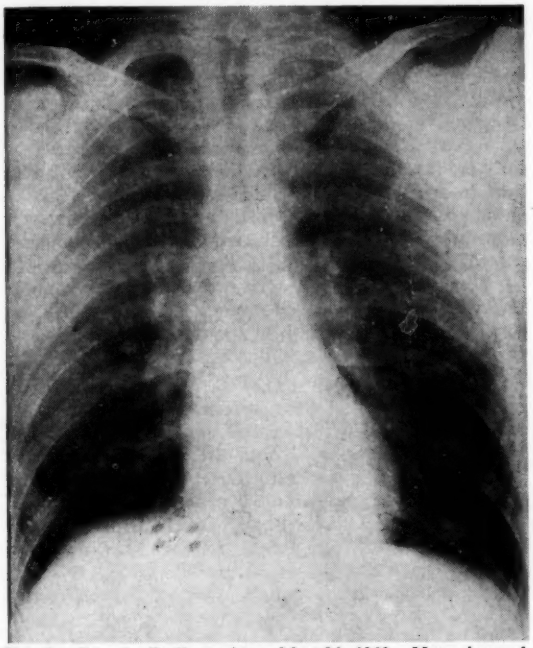

FIG. 2.—Case 3. Radiograph on May 26, 1950. Note size and distribution of opacities.

Other cases of disseminated pneumonia were not quite as striking.

Case 8.—Man aged 37; contact of his three children, all suffering from chicken-pox. August 26, 1958: appearance of rash and cough. Progressively worse; admitted on August 31. *X*-ray examination showed "miliary" mottling of both lung fields. Scanty mucoid sputum, no pathogens isolated on culture. On 12th day of illness developed thrombophlebitis of left calf and had a two-weeks course of anticoagulants (phenindione). September 30: *x*-ray examination at follow-up showed generalized increase in lung markings.

In Case 5 disseminated pneumonia was associated with visceral chicken-pox, in case 7 with meningo-encephalitis, in Case 9 with varicella gangrenosa, and in Case 12 with herpes zoster.

Neurological Complications

Neurological complications may precede, accompany, or follow the development of the rash up to 21 days. In the five cases in the present series, onset of encephalitic symptoms occurred one, three, six, and seven days after the rash and preceded the rash by three days in one case. The case report of the child who died was as follows:

Case 10.—Boy aged 6, admitted June 3, 1959, seven days after onset of varicella. Vomiting had started two days prior to admission. Drowsy for one day when admitted. On examination: semicomatose, restless, dehydrated. Skin: sparse lesions which were haemorrhagic. Chest clear on auscultation, no cardiac murmurs. Blood-pressure 105/50. C.N.S.: pupils dilated, reaction to light doubtful, marked photophobia; no neck rigidity. Negative Kernig and Brudzinski's signs. Normal reflexes. Sensorium could not be tested. C.S.F. pressure 80 mm., clear, no increase in cells or protein. Blood urea and electrolytes within normal limits. White blood count, 16,300/c.mm. (73% polymorphs, 23% lymphocytes, 4% monocytes). Prophylactic treatment with penicillin started. 2½ pints (1.3 litres) dextrose 5% to combat dehydration administered, but steady deterioration continued. Tracheostomy performed when left lung apparently collapsed owing to aspiration of vomit. Temperature rose to 103° F. (39.5° C.); died less than 24 hours after admission. At necropsy: brain swollen, vessels engorged, parenchyma bulging. Microscopically: widespread swelling of capillary endothelium, but no haemorrhages. Lungs congested, with areas of collapse. The air passages contained mucus and slightly blood-stained oedema fluid; scattered petechial haemorrhages on pleurae. Congestion of alimentary tract. No other abnormality. Cause of death: cardio-respiratory failure secondary to encephalitis following chicken-pox.

The next case report illustrates the seriousness of neurological complications in an adult.

Case 7.—Man aged 46; admission July 22, 1957, as case of meningitis with two days' history of pyrexia, headache, and vomiting of sudden onset. On examination—rather ill, lethargic, a few macules on trunk. C.N.S.: signs of meningitis. C.S.F.: cells 133 (polymorphs 22, lymphocytes 111); protein, 36 mg./100 ml.; chlorides, 550 mg./100 ml.; sugar, 68 mg./100 ml. Phenoxymethylpenicillin injections started. July 23: varicella rash. Photophobia and meningism marked. No cough, chest *x*-ray film showed mild disseminated pneumonia; semiconscious. July 25: nearly comatose; reacts only to painful stimuli; has to be fed by Ryle's tube. C.S.F.: cells 1,500 (polymorphs 1%, lymphocytes 75%, monocytes 24%); protein 750 mg./100 ml.; chlorides and sugar normal. July 26: recovered consciousness with complete amnesia of previous three days. Slow uneventful recovery. C.S.F. normal on October 30.

All other cases in this group had less severe symptoms with only slight pleocytosis and/or raised protein in the C.S.F., but the following case was of some interest.

Case 1.—A girl aged 5 developed an asymmetrical spastic paraplegia in March, 1950, seven days after appearance of varicella rash. She also had generalized hyperreflexia, marked clonus, and profuse vomiting. C.S.F. was under increased pressure but contained only 57 cells (all lymphocytes) and protein 35 mg./100 ml. Discharged after one month, walking normally, but some ankle clonus still present.

Varicella Gangrenosa

One patient developed varicella gangrenosa.

Case 9.—A 9-year-old boy admitted on December 16, 1958, had four deep necrotic ulcers each about 1–1½ in. (2.5–3.8 cm.) in diameter—two on buttocks, one on abdomen, and one on thigh. No pathogens isolated from the lesions; general condition remarkably good. Lesions healed slowly by granulation, leaving deep scars.

Herpes Zoster

Herpes zoster is occasionally associated with chicken-pox. It may arise as a subsequent complication or precede varicella as in the following patient who had never had varicella or zoster.

Case 11.—A man aged 85, admitted on June 10, 1959, afebrile, yet extremely ill with severe herpes zoster affecting all three trigeminal branches on the left. There was corneal ulceration and chemosis. Herpes lesions were superinfected with *Staph. aureus* and *Proteus sp.* Typical varicella rash with lesions on buccal mucosa and fauces had developed three days after onset of zoster. Fifteen days after admission, while improving, he developed a large pulmonary infarct. Anticoagulant therapy (phenindione) was given for one month with satisfactory clearing of pulmonary lesion.

Pulmonary Infarction

The following case of multiple bilateral pulmonary infarcts proved fatal.

Case 4.—Man aged 34 developed mild varicella on January 6, 1954. Haemoptysis two weeks later, followed by polyuria and macroscopic haematuria. February 9: pains in chest and dyspnoea, rapidly increasing in severity. On admission, February 16, found to be very ill, dyspnoeic, febrile (101.2° F. 38.4° C.). Recently healed chicken-pox lesions on body. Blood-pressure 130/90, gallop rhythm. *X*-ray examination confirmed bilateral pleural effusions, which on aspiration were found to be heavily blood-stained. After aspiration *x*-ray film showed opacities suggestive of multiple pulmonary infarcts. Blood count and blood urea normal. R.B.C. in urine. After initial slight improvement patient died suddenly on February 22. Necropsy: Ulcerated varicella lesions underneath left scrotum, which appeared bruised; from these, thrombosis of spermatic veins, iliac veins, and inferior vena cava, giving rise to bilateral pulmonary emboli and pulmonary infarction. Cause of death: cardio-respiratory failure due to multiple pulmonary infarcts.

Visceral Involvement

To end this series of case histories, a case of extensive haemorrhagic chicken-pox with visceral involvement is described. The extent of the lesions as well as their microscopical appearance would justify the term "visceral chicken-pox." This case closely resembled that of visceral herpes zoster described by Wyburn-Mason (1957).

Case 5.—Baby girl aged 1, admitted July 10, 1957, from a poor home in neglected condition. On admission, widespread haemorrhagic gangrenous varicella rash. Temperature 101.8° F. (38.8° C.); haemoglobin, 57%; white blood count, 7,100 (polymorphs 52%, lymphocytes 48%). In spite of high dosage of penicillin, and later addition of chloramphenicol, temperature rose gradually to 104° F. (40° C.) on July 17 and she died. Necropsy: Respiratory system: varicella lesions covering the pharynx, epiglottis, vocal cords, and trachea down to the third ring. Trachea and main bronchi contained mucus and aspirated vomit. Right upper lobe somewhat collapsed, both lungs congested and oedematous. Alimentary system: mouth, tongue, and pharynx showed ulcerated vesicles not extending into stomach. Small and large bowel appeared normal. Skull and its contents were, unfortunately, not examined. Microscopically the tongue, epiglottis, larynx, and lungs showed scattered necrotic and ulcerated lesions on their epithelial surfaces. Oedema of lungs and bronchopneumonic changes. One large pulmonary vessel contained an ante-mortem thrombus. Cause of death: varicella haemorrhagica and aspirative pneumonia.

Discussion

Though adults seldom suffer from chicken-pox, it appears that complications are more common and more severe than in children (Davidson, 1956). In the present series, 6 out of 12 patients were adults. Boucher (1953), Saslaw *et al.* (1953), Lander (1955), Tan *et al.* (1956), and McLachlan (1957) have reported similar findings.

Disseminated pneumonia caused by the virus of varicella has been previously described (Saslaw *et al.*, 1953; McLachlan, 1953; Tan *et al.*, 1956; Southard, 1956; *British Medical Journal*, 1957). It is a diffuse pneumonia with very characteristic radiological appearances. Widespread nodular shadows are seen, similar to, but larger than, those of miliary tuberculosis, superimposed on increased bronchovascular markings. There is usually no segmental consolidation or collapse. Resolution starts 10 to 14 days after onset and is progressive. In most of our cases, however, increased bronchovascular markings were still visible up to two months afterwards. Chicken-pox pneumonia usually develops in adults only. Occasionally disseminated pneumonia is diagnosed on radiological grounds only, as clinical symptoms such as cough and sputum are often mild or absent.

A point of interest is the frequent association of a profuse skin rash with disseminated pneumonia, while symptoms of encephalitis seem to occur more often in patients with a sparse rash. In the present series there were no fatal cases due to disseminated pneumonia. Corticosteroids appear to enhance the action of varicella virus, and it is in cases receiving corticosteroids that the only fatalities from disseminated pneumonia had been recorded (Cheatham *et al.*, 1956; *Lancet*, 1957; *British Medical Journal*, 1957; Harrison, 1957; McLachlan, 1957; Stokes, 1959a, 1959b). It therefore appears that corticosteroids should be discontinued in patients developing chicken-pox and adequate antibiotic cover given.

The most serious complication of chicken-pox is encephalitis. The incidence has been estimated at about 1 in 1,000 (Miller *et al.*, 1956). Mortality varies between 10 and 50%. The patients who recover do so usually without sequelae and within two to three weeks. The encephalitis of chicken-pox is non-specific and indistinguishable from that following measles or rubella: the theory has been postulated that it is an allergic reaction in the central nervous system (Russell, 1955).

Encephalitis presents clinically either as (1) meningo-encephalitis or (2) encephalomyelitis, and histologically as either haemorrhagic leucoencephalitis or acute disseminated encephalomyelitis. The two forms are probably only variants of one pathological process (Russell, 1955).

The onset of encephalitis may precede the rash by up to four days as in Case 7, or follow it by up to 21 days. Among all the reported cases surveyed, encephalitis developed an average of six days after the appearance of the rash. The onset is gradual, with headache and meningeal signs, focal neurological signs being usually absent. Drowsiness and stupor are present in about half the cases. When the onset is sudden, with convulsions and coma, the prognosis is bad. Such a case was encountered in the present series, a boy of 6 who died within three days (Case 10). The C.S.F. is usually clear but under increased pressure: it can be either completely normal or show a lymphocytic pleocytosis with or without increase in protein content.

Histologically, in acute disseminated encephalomyelitis, there is widespread perivenous inflammatory cell infiltration and demyelination with general survival of nerve cells even within the inflamed area (*Lancet*, 1957), which might explain the recovery without sequelae. In haemorrhagic leucoencephalitis there are macroscopical widespread petechial haemorrhages throughout the white matter and microscopical swelling of capillary

endothelium in grey and white matter. Some necrosis of vessel walls occurs with proliferation of microglia and occasional formation of glial nodules. Perivascular demyelination and round-cell cuffing are demonstrable (Miller *et al.*, 1956).

A fatal case of acute haemorrhagic leucoencephalitis has been described by Lander (1955). Bergman and Magnusson reported 10 cases with neurological complications occurring in the decade 1927 to 1938 at Stockholm. In England and Wales nine cases were reported in 1950, one of which was fatal (quoted from Miller *et al.*, 1956). The present survey adds five cases with neurological complications. Four of these were in children aged 4–15 years; one terminated fatally. These findings are similar to those described by Brain (1955). Lesions suggestive of cerebellar involvement, as described by Walsh (1957), were not seen.

The occasional association between chicken-pox and shingles has been widely discussed. The identity of the viruses of varicella and zoster has now been established by antigenic analysis and by antibody evidence (Hope Simpson, 1954; *Lancet*, 1954; Downie, 1955; Stokes, 1959a, 1959b).

It is not clear which factors determine whether one or the other disease appears after exposure to the virus or, if both appear, which one arises first. Stokes (1959) has discussed the theories that varicella virus possesses neurotropic properties, and that varicella can be regarded as the early general infection while zoster is a late localized manifestation in the immune or partially immune person at a later age. These theories would not explain the development of the chicken-pox rash three and seven days respectively after the onset of zoster in two of our elderly patients, and in two cases of Knyvett *et al.* (1957).

Severe visceral involvement will occasionally occur and is usually fatal (one case reported by Johnson (1940), three cases by Nicolaides (1957), one case in the present series). In all cases there was extensive involvement of the oesophageal mucosa down to the cardia and of the laryngeal mucosa down into the main bronchi, as well as on the pleurae. Macroscopically, there are vasodilatation and oedema, haemorrhages, and inflammatory changes which predispose to vascular thrombosis. Microscopically, cells of the epithelial types are mainly affected, preceded by involvement of the endothelial cells. Case 5 in this series presented these findings.

A rare complication of chicken-pox is varicella haemorrhagica, the aetiology of which is ill understood. A case has been described by Cohen and Bansmer (1947) of a boy of 11 who developed varicella haemorrhagica and purpura and recovered after 30 days in hospital. Treatment included transfusions and analeptics. The case was seen in the acute stage by Dr. William Dameshek, who found it to be indistinguishable from idiopathic thrombocytopenic purpura, and perhaps patients with varicella haemorrhagica develop this abnormality temporarily. The incidence of this complication is low and only single cases have been reported. The mortality is high—only three out of nine cases have recovered. In no case was there a previous history of bleeding or haemorrhagic diathesis. In our two cases of varicella haemorrhagica (Cases 5 and 10), one was a baby from whom no blood was taken for extensive haematological studies, and the other was a boy of 6 who died within 24 hours of admission.

Ocular involvement occasionally occurs in chicken-pox. Conjunctivitis, and punctate and interstitial keratitis have been described (Walsh, 1957). The ocular complications are usually mild and the recovery rate is high. Walsh also describes the case of a 5-year-old girl in whom a bilateral optic neuritis with practically total loss of vision developed a week before the appearance of the varicella rash. He also describes other cases in which transient blindness occurred shortly after an attack of chicken-pox. Similarly, Hatch (1949) reported another case of bilateral optic neuritis which followed varicella, and cases of varicella of the cornea have been described (Pickard, 1936). No ocular involvement occurred in our series except in Case 11, who had ulceration of the cornea due to zoster of the ophthalmic branch of the trigeminus.

Summary

Twelve patients with complications of varicella were admitted to the Leicester Isolation Hospital over the decade 1950 to 1959. The age of the patients ranged from 1 to 85 years. The commonest complications were disseminated pneumonia, which presented a characteristic radiological appearance, and encephalitis. The rarest was varicella haemorrhagica. There were three fatal cases.

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References

Boucher, P. R. (1953). *Lancet*, **1**, 854.
Brain, Sir Russell (1955). *Diseases of the Nervous System*, p. 506. Oxford Univ. Press, London.
Brit. med. J., 1957, **1**, 511.
Cheatham, W. J., Weller, T. H., Dolan, T. F., jun., and Dower, J. C. (1956). *Amer. J. Path.*, **32**, 1015.
Cohen, J. J., and Bansmer, C. (1947). *New Engl. J. Med.*, **237**, 222.
Davidson, Sir Stanley (1956). *Principles and Practice of Medicine*, 3rd ed., p. 36. Livingstone, Edinburgh.
Downie, A. W (1955). *Lancet*, **1**, 544.
Harrison, M. T. (1957). Ibid., **2**, 542.
Hatch, H. A. (1949). *J. Pediat.*, **34**, 758.
Hope Simpson, R. E. (1954). *Lancet*, **2**, 1299.
Johnson, H. N. (1940). *Arch. Path. (Chicago)*, **30**, 292.
Knyvett, A. F. (1957). *Med. J. Aust.*, **1**, 91.
Lancet, 1954, **2**, 1314.
—— 1957, **2**, 839.
Lander, H. (1955). *J. Path. Bact.*, **70**, 157.
McLachlan, I. M. (1953). *Lancet*, **1**, 1152.
—— (1957). Ibid., **2**, 492.
Miller, H. G., Stanton, J. B., and Gibbons, J. L. (1956). *Quart. J. Med.*, **25**, 427.
Nicolaides, N. J. (1957). *Med. J. Aust.*, **2**, 88.
Pickard, R. (1936). *Brit. J. Ophthal.*, **20**, 15.
Russell, D. S. (1955). *Brain*, **78**, 369.
Saslaw, S., Prior, J. A., Wiseman, B. K. (1953). *Arch. intern. Med.*, **91**, 35.
Southard, M. E. (1956). *Amer. J. Roentgenol.*, **76**, 533.
Stokes, J., jun. (1959a). In *Viral and Rickettsial Infections of Man*, edited by T. M. Rivers and F. L. Horsfall, jun., 3rd edition, p. 773. Pitman Medical Publishing Co., London.
—— (1959b). In *Textbook of Medicine*, R. L. Cecil and R. F. Loeb, 10th ed., p. 28. Saunders, Philadelphia.
Tan, D. Y. M., Kaufman, S. A., and Levene, G. (1956). *Amer. J. Roentgenol.*, **76**, 527.
Walsh, F. R. (1957). *Clinical Neuro-ophthalmology*, 2nd ed. Williams and Wilkins, Baltimore.
Wyburn-Mason, R. (1957). *Brit. med. J.*, **1**, 678.

" Dr. Janet Travell is not after all the first woman to be the White House physician. That distinction belongs to Dr. Susan Ann Edson, who attended President Garfield from the time when he was shot on July 2, 1881, until he died on September 19. Dr. Edson was Garfield's family doctor, and she was known at the White House as the ' head nurse.' Her devoted service during Garfield's last days undermined her own health, and she was given a special grant of $3,000 by Congress." (*Daily Telegraph*, March 2.)

PELVIC ABNORMALITIES IN MONGOLS

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Caffey and Ross (1956) first observed that the radiological appearances of the pelvis in mongols were abnormal. Kaufmann and Pelargonio (1957) confirmed this original observation, which was later extended to include the detailed study of more subjects (Caffey and Ross, 1958). This paper describes our findings in a further series of 57 mongols whom we have examined radiologically since 1956. During this period of observation four infant mongols died and went to necropsy. The data which were obtained demonstrate that characteristic anatomical configurations of the pelvic girdle appear frequently in these individuals. The superior iliac spine is absent and the wing of the os ilium is widely splayed, causing a decrease in the cephalo-caudal diameter (Fig. 1). The acetabular and iliac angles are decreased and there is a low iliac index (Fig. 2). The iliac index (I.I.) is defined as the sum of

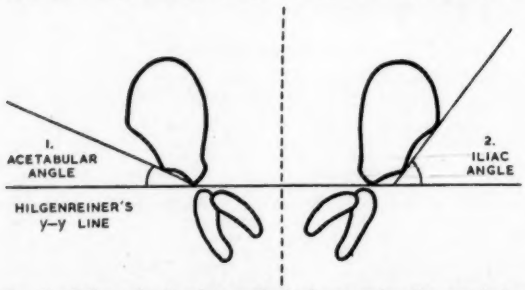

FIG. 2.—Schematic drawing method of measuring the acetabular and iliac angles. Both angles are based on Hilgenreiner's line extending through both Y-cartilages.

both acetabular angles (A.A.) and both iliac angles (I.A.) divided by two. The ramus of the ischium is abnormal in length and tapers at the distal end, while in infants of 9 months or more the femur often shows a valgus deformity.

X-ray Examinations

Our series of 57 mongols was divided into two groups and these were studied separately. (1) Infants: The methods described by Caffey and Ross (1956) were employed in the examination of the 43 *x*-ray films obtained from 34 mongols under 1 year of age. Measurements of the A.A. and the I.A. were made and the I.I. was calculated. (2) Older infants, children, and young adults: In this group were 23 mongols, aged 1 to 22 years, who, apart from their basic disorder, were essentially healthy. Most of the older ones were attending the local training school for the mentally handicapped, though some were living at home.

Necropsy Examinations

The post-mortem findings in the four mongols who died were compared with those in seven normal newborn babies or infants of similar ages. The mongols were aged 1 day, 3 weeks, 3½ and 6 months at the time of death. Particular attention was given to the bones of the pelvis, the lumbar region of the spinal column, and the femora. Specimens were preserved in 4% formalin and radiographs of the pelvis were taken both before and after the injection of 20% lipiodol into both hip-joints. The exact positions of the pelvic bones relative to one another were studied carefully, attention being focused on the same fixed points in different views.

Results

Of the 34 infants (Group 1) examined, three had been born prematurely. Their birth weights were 1,270 g., 1,630 g., and 1,900 g., and their respective measurements were: A.A., 15, 9, and 9 degrees; I.A., 45, 40, and 43 degrees; I.I., 60, 49, and 52. The data presented by the entire group of 34 infants were in full agreement with the characteristic patterns that have already been described. The mean values revealed were A.A. 14 degrees, I.A. 42 degrees, and I.I. 50, compared with the average figure, A.A. 25–28 degrees, I.A. 55–58 degrees, and I.I. 79–81 for the normal infants.

In the second group the same characteristic changes were evident. In one child who was radiographed at 2 years of age and again at 11 years the abnormalities had neither changed in character nor progressed in degree.

The radiological appearances of the four necropsy specimens demonstrated the same anomalies that had been observed in living subjects, and differed in appearance from the necropsy specimens of normal infants. The arthrograms did not reveal any abnormality.

The changes that have been noted are well illustrated in the photographs (Fig. 3). The pelvis of the mongol is contrasted with the normal pelvis in the antero-posterior view (Fig. 3 A), in the lateral view (Fig. 3 B), and in the cephalo-caudal view (Fig. 3 C). In the antero-posterior view the ilium has wide laterally flared wings with a reduced cephalo-caudal projection. The

FIG. 1.—Characteristic *x*-ray appearance of the "**mongol pelvis**" at different ages. A, 1 day old; B, 1½ years old; and C, 16 years old.

superior iliac spine is absent, and the ischium appears to be elongated. In the other views, also, it is the ilium which appears to be abnormal.

Discussion

Our studies confirm that radiological changes are seen in the pelvis of 4 out of 5 mongols. These anomalies are characteristic of both premature and newborn mongol infants, and are of particular diagnostic significance. The appearances persist into adult life, and further study of *x*-ray films in adult mongols is obviously indicated. It appears that all who have investigated this problem agree that the *x*-ray changes are diagnostic of mongolism, and it seems justifiable to postulate the concept of a true "mongol pelvis."

We have evidence that adult mongols can develop dislocation of the hip, and have observed three cases in 18 mongols over 5 years of age. This finding is perplexing, because the appearances in the "mongol pelvis" are the opposite of those seen in congenital dislocation of the hip. We consider that the dislocation of the hip observed in the mongol patient is of a secondary nature, such as that which follows in patients with paralytic poliomyelitis, spina bifida, and spastic diplegia or paraplegia.

We believe that the radiological and anatomical findings could be due to a developmental anomaly of the pelvic girdle which affects the configuration of the ilium, but the possibility that an abnormality of form due to irregular growth as an additional factor cannot be excluded. Further studies are to be undertaken in order to make this point clearer. It is our opinion that the well-known generalized hypotonic musculature in mongolism does not contribute towards the development of these abnormalities. The fact that we have noted two cases of amyotonia congenita in which the *x*-ray film of the pelvis was completely normal lends support to this view. In discussing the possible causes of these pelvic changes we must consider other congenital abnormalities which have been reported in the mongol. Lejeune *et al.* (1959) and Jacobs *et al.* (1959) demonstrated an extra autosomal chromosome pattern in mongols. These findings have been confirmed by Ford *et al.* (1959) and by Böök *et al.* (1959). It may be that the presence of an extra chromosome is instrumental in causing the pelvic manifestations which we have emphasized. The means by which this can be brought about is unknown, but it may be of value to investigate the appearance of the pelvis on *x*-ray examination in other conditions in which an abnormal chromosomal composition is established.

Summary

Characteristic variations from the normal which were observed in the *x*-ray films of the pelvic bones of over 60 mongols are reviewed. These changes are constant from birth onwards and persist throughout life without signs of any progression in severity.

In three adult mongols dislocation of the hip, which is considered to be a secondary phenomenon, is recorded.

Anatomical studies establish the precise nature of the pelvic anomaly and indicate that the abnormal appearances are due particularly to the configuration of the os ilium.

References

Böök, J. A., Fraccaro, M., and Lindsten, J. (1959). *Acta paediat. (Uppsala)*, **48**, 453.
Caffey, J., and Ross, S. (1956). *Pediatrics*, **17**, 642.
——— (1958). *Amer. J. Roentgenol.*, **80**, 458.
Ford, C. E., Jones, K. W., Miller, O. J., Mittwoch, U., Penrose, L. S., Ridler, M., and Shapiro, A. (1959). *Lancet*, **1**, 709.
Jacobs, P. A., Baikie, A. G., Court Brown, W. M., and Strong, J. A. (1959). Ibid., **1**, 710.
Kaufmann, H. J., and Pelargonio, S. (1957). *Schweiz. med. Wschr.*, **87**, 1529.
Lejeune, J., Gautier, M., and Turpin, R. (1959). *C.R. Acad. Sci. (Paris)*, **248**, 602, 1721.

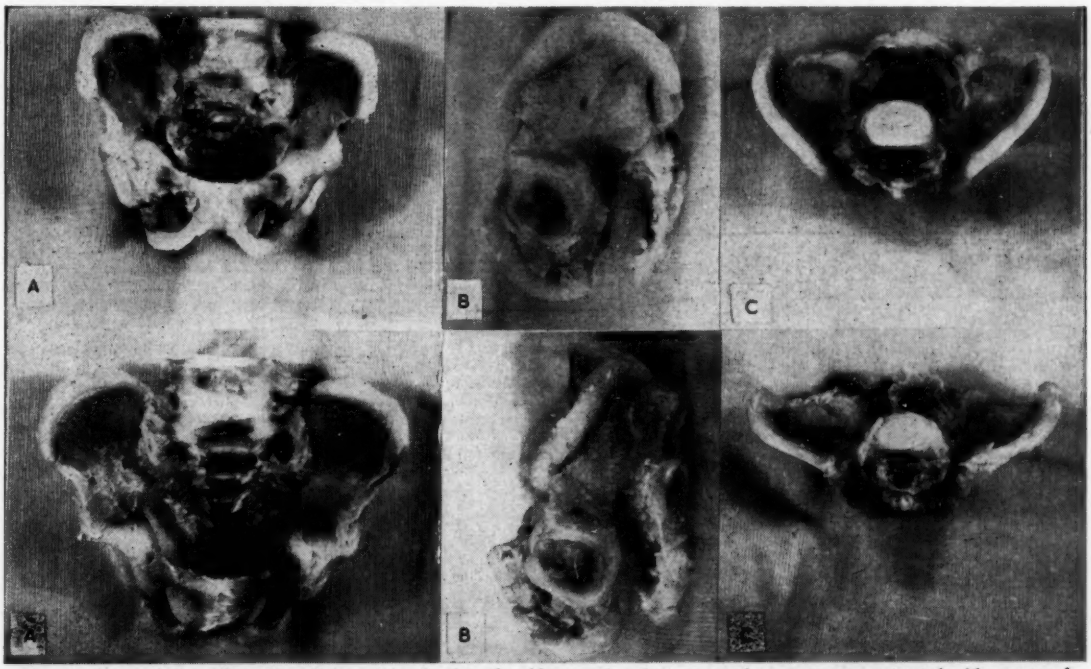

FIG. 3.—Anatomical configuration of the pelvis of a 3-weeks-old mongol patient removed at necropsy contrasted with a normal pelvis. A, Antero-posterior view. B, Lateral view. C, cephalo-caudal view. Upper row: Normal pelvis. Lower row: "Mongol pelvis." Note: in A and C the opening of the wings of the ilium causing the broader appearance, visible on the *x*-ray films; and in B the angulation and downward slope of the iliac wing in the "mongol pelvis."

Medical Memoranda

Comparison of the Effects of Three Rauwolfia Alkaloids in Hypertension

The rauwolfia alkaloid reserpine has been shown to produce a significant fall in blood-pressure in patients with essential hypertension (Cooper and Cranston, 1957). However, reserpine has from time to time produced unpleasant and sometimes severe side-effects, notably depression or frank psychosis (*Brit. med. J.*, 1955). It has been suggested that other rauwolfia alkaloids, such as rescinnamine, have equally satisfactory hypotensive properties, but might not have the side-effects of reserpine (Smirk and McQueen, 1955). For this reason a small controlled trial has been carried out, to compare the hypotensive properties and side-effects of the rauwolfia alkaloids reserpine, rescinnamine, and deserpidine.

METHODS

The series consisted of five men and five women whose ages ranged from 26 to 62, all of whom were thought to have essential hypertension. They all received reserpine, rescinnamine, deserpidine, in doses of 0.5 mg. t.d.s., 0.75 mg. t.d.s., and 1.0 mg. t.d.s., and inert control tablets. The drugs and control tablets were identical, so that neither the patient nor the examiner knew which tablet was being taken, and the drug order was randomized. Each patient was treated for 12 consecutive weeks with each tablet, and attended once weekly, at the same time of day on each occasion. Because the effectiveness of these drugs was uncertain, and because regular attendance over a long period was necessary for the trial, only patients with mild hypertension were included. Blood-pressures were measured by the same person with the same sphygmomanometer each time, in both the lying and the standing position. The readings during the first six weeks of each trial were ignored, so as to exclude errors due to delayed hypotensive action both from overlap from the previous trial and of the drug in use in any one trial period.

None of the patients had any family or personal history of depression, anxiety, or other mental illness, and their nasal airways were not congested at the beginning of the trial. At each attendance they were weighed, and questioned about nasal congestion, tiredness, depression, and appetite. The data for the last six weeks of each period were used for comparison.

RESULTS

Blood-pressure.—For each patient the mean level was calculated with its standard error, for the last six weeks of each period, in the standing and lying positions. The mean levels during the control period and the mean fall in blood-pressure during the second six weeks of treatment with reserpine, rescinnamine, and deserpidine are shown in Table I. Reserpine produced a significant fall in blood-pressure in seven of the patients, and its overall effect was highly significant. The mean fall was $12.08 \pm 2.56/13.33 \pm 2.35$ mm. Hg in the lying. $16.00 \pm 3.34/15.04 \pm 3.43$ mm. Hg in the standing position. Deserpidine produced a significant fall in blood-pressure in five patients. The hypotensive action was less consistent than that of reserpine. The mean fall was $9.59 \pm 5.46/10.93 \pm 3.98$ mm. Hg in the lying, $10.96 \pm 5.93/11.23 \pm 3.10$ mm. Hg in the standing position. The fall in systolic blood-pressure in both positions is not significant. The fall in diastolic pressure is less than that seen with reserpine. Rescinnamine produced a significant fall in blood-pressure in only four patients. The hypotensive action was so marked in these patients that the mean fall for the whole group was $12.73 \pm 4.75/10.27 \pm 2.48$ mm. Hg in the lying, $11.78 \pm 5.50/9.96 \pm 2.53$ mm. Hg in the standing position.

Side-effects.—These were recorded as none, slight, or marked. The only mental changes observed were depression and/or tiredness. The results are summarized in Table II. There is no clear correlation between observed mental changes and nasal congestion. Neither do the side-effects occur only in patients with a significant fall in blood-pressure. The number of patients is small, but it would appear that side-effects occur more often in those treated with reserpine than in those on

TABLE I.—*Effect of Three Rauwolfia Alkaloids in Essential Hypertension*

No.	Age and Sex	Position	Control	Fall in Blood-pressure		
				Control–Reserpine	Control–Deserpidine	Control–Rescinnamine
5	26 M	Lying	160·8 ± 4·73/111·7 ± 4·01	17·3/25·4	14·8/19·1	5·6/14·0
		Standing	165·0 ± 4·83/115·8 ± 2·71	29·8/26·1	25·0/13·8	5·3/8·3
3	57 F	Lying	151·3 ± 3·71/83·5 ± 2·51	22·3/10·8	7·0/8·0	20·6/6·0
		Standing	138·5 ± 3·69/82·7 ± 1·35	6·2/3·6	−5·8/+1·4	7·6/0
7	33 M	Lying	153·8 ± 7·35/113·3 ± 4·21	23·3/22·2	36·3/26·1	31·1/18·3
		Standing	147·5 ± 7·16/116·7 ± 5·1	27·3/26·9	29·7/28·7	22·5/15·0
6	57 F	Lying	263·7 ± 2·74/133·8 ± 2·46	9·7/19·1	34·9/21·6	44·5/27·1
		Standing	249·5 ± 3·74/130·3 ± 2·91	27·7/28·8	46·5/25·0	51·2/28·6
8	62 M	Lying	188·3 ± 3·85/102·0 ± 2·22	20·8/13·7	0·8/2·5	10·3/4·0
		Standing	191·5 ± 7·35/106·0 ± 3·98	21·5/8·2	1·5/2·8	21·0/9·7
18	51 M	Lying	174·8 ± 3·25/95·4 ± 5·05	3·2/5·4	3·6/4·6	+0·5/−4·1
		Standing	166·0 ± 5·10/102·4 ± 2·02	4·0/16·4	−1·3/+14·2	−3·7/+3·2
13	57 F	Lying	182·7 ± 6·49/108·2 ± 3·75	3·9/3·5	−5·3/+0·9	4·4/5·7
		Standing	187·3 ± 5·55/112·8 ± 3·35	12·3/10·1	−2·2/+4·6	11·6/5·6
10	55 F	Lying	201·8 ± 5·12/96·0 ± 2·45	10·0/15·7	21·3/18·5	9·4/10·2
		Standing	200·2 ± 5·89/103·8 ± 4·20	18·0/23·5	24·7/15·3	6·8/14·4
12	62 F	Lying	159·5 ± 3·97/90·0 ± 2·56	4·0/5·2	0/1·3	−3·8/+9·0
		Standing	156·3 ± 2·35/86·8 ± 2·46	0/−2·0	0·5/3·0	−13·5/+5·8
2	54 M	Lying	153·0/100·0	6·3/12·3	−17·5/+6·7	4·7/12·5
		Standing	154·0/99·0	13·2/8·8	−9·0/+3·5	9·0/9·0
		Mean lying		12·08 ± 2·56/13·33 ± 2·35	9·59 ± 5·46/10·93 ± 3·98	12·73 ± 4·75/10·27 ± 2·48
		Mean standing		16·00 ± 3·34/15·04 ± 3·43	10·96 ± 5·93/11·23 ± 3·10	11·78 ± 5·50/ 9·96 ± 2·53

control tablets, and that side-effects occur no more frequently in patients treated with rescinnamine and deserpidine than in those on control tablets.

TABLE II

Drug	Mental Changes, Tiredness, or Depression			Nasal Congestion		
	Marked	Slight	None	Marked	Slight	None
Reserpine ..	2	4	4	3	3	4
Rescinnamine ..	0	1	9	1	3	6
Deserpidine ..	0	4	6	1	3	6
Control	1	2	7	1	3	6

TABLE III

Drug	Appetite		Weight		
	Increase	Normal	Increase	Stationary	Loss
Reserpine ..	4	6	3	4	3
Rescinnamine	2	8	4	1	5
Deserpidine ..	3	7	3	3	4
Control ..	0	10	4	3	3

Weight and Appetite.—In this series the weight changes were variable, and there was no correlation between the subjective impression of appetite, and weight changes. The results are summarized in Table III. The changes in weight show no striking differences in the four trials, whereas there appears to be a slight subjective feeling of increased appetite when the patients were treated with rauwolfia alkaloids.

COMMENT

The blood-pressure levels were relatively stable in each patient, as shown by the small standard error of the means during each period. Reserpine produced a fall of diastolic blood-pressure in 10 patients in the lying and in nine in the standing position, while it produced a fall in systolic pressure in 10 patients in the lying and in nine in the standing position. Rescinnamine caused a fall in diastolic blood-pressure in nine patients in the lying and in nine in the standing position, while it produced a significant fall in systolic blood-pressure in nine patients in the lying and in seven in the standing position. Deserpidine caused a fall in diastolic blood-pressure in 10 in the lying and in 10 in the standing position, while it produced a fall in systolic pressure in six in the lying and in six in the standing position. This confirms the observation of Cooper and Cranston (1957) that reserpine, in a dose of 0.5 mg. thrice daily, almost invariably, and usually significantly, lowers the blood-pressure. Rescinnamine, in a dose of 0.75 mg. thrice daily, and deserpidine, in a dose of 1 mg. thrice daily, sometimes lower the blood-pressure and on occasion significantly and markedly, but the effect is not predictable.

Though the overall diastolic fall in blood-pressure produced by rescinnamine and deserpidine is very similar and less than that produced by reserpine, the fall in the individual patient varies greatly. The observations on side-effects suggest that they are more likely to occur when the patient is receiving reserpine than when he is being treated with rescinnamine or deserpidine in these doses. In this series none of the three drugs had any consistent effect on the patients' weights.

The conclusion one may draw from the results of this trial is that of the three rauwolfia alkaloids in these doses reserpine is the drug of choice because of its predictable effect on the blood-pressure. If the side-effects from reserpine are troublesome, it is worth trying the effect of rescinnamine or deserpidine, which may produce a satisfactory fall in blood-pressure even though the effectiveness of the drug in the individual patient cannot be predicted but must be discovered by trial and error.

SUMMARY

The effects on the blood-pressure of the three rauwolfia alkaloids—reserpine, rescinnamine, and deserpidine—have been compared in a small controlled trial of 10 patients with essential hypertension. The side-effects of the three drugs were observed.

Reserpine, in a dose of 0.5 mg. thrice daily, produced a predictable fall of blood-pressure in all the patients. Rescinnamine in a dose of 0.75 mg. thrice daily, and deserpidine in a dose of 1 mg. thrice daily, produced a significant fall of blood-pressure in some patients, but this effect was not predictable. Reserpine appears to produce side-effects more often than rescinnamine and deserpidine.

Of the three alkaloids, reserpine is the drug of choice, but if the side-effects are troublesome it is worth trying rescinnamine or deserpidine, which may produce a substantial but not predictable fall in blood-pressure.

We thank Dr. G. St. John Ives for generously allowing us to use his surgery at Thame, and the matron of Didcot Cottage Hospital for the use of rooms in the out-patient department, for the purpose of following up the patients who lived in these areas. We are grateful to Dr. C. D. Faulkner, of Ciba Ltd., for supplying the drugs and the control tablets for the trial.

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REFERENCES

Brit. med. J., 1955, **2**, 1378.
Cooper, E. H., and Cranston, W. I. (1957). *Lancet*, **1**, 396.
Smirk, F. H., and McQueen, E. G. (1955). Ibid., **2**, 115.

"[It was at one time the custom in the Western Province of Tanganyika to treat] the young victims of smallpox by hyperextension and traction of both elbows and also sometimes of both ankles until they 'cracked.' The object of this painful procedure was to 'bring out the rash' satisfactorily and so to safeguard the life of the patient. Last year, when visiting one of the mission bedded dispensaries, the nursing sister asked me to see a case of smallpox in a small boy. She was puzzled because the patient, who was by now recovering from the smallpox, had fracture dislocation of both elbows. The parents told me rather shamefacedly that the child's grandparents had taken charge of the patient and had insisted on applying the old treatment. I was reminded again of this barbarous custom a few weeks ago. A very old African woman was admitted with pneumonia, and while feeling for her wrist under the blanket to take her pulse I found she could not extend the arm, which was ankylosed at the elbow at about a right angle. When I asked her the reason for the deformity she whispered 'smallpox'; and her deeply pock-marked face showed that without doubt she had at some time suffered from severe smallpox. The custom of treating smallpox in this way is fortunately disappearing and may not be known to many medical practitioners, but it is recorded as a matter of interest." (Dr. A. J. Keevill in *East African Medical Journal*, October, 1960.)

Reviews

HOSPITAL INFECTION

Hospital Infection. Causes and Prevention. By R. E. O. Williams, M.D., M.R.C.P., R. Blowers, M.D., L. P. Garrod, M.D., F.R.C.P., and R. A. Shooter, M.D. (Pp. 307+x; illustrated. 35s.) London: Lloyd-Luke (Medical Books) Ltd. 1960.

Though it has been known for nearly a century that cross-infection occurs in hospitals, no adequate summary of its causation and prevention has so far appeared. This volume, written jointly by four recognized authorities, fills this gap admirably. Its first half gives an account of what is known of the sources and modes of transmission of cross-infection in which gastro-intestinal, genito-urinary, puerperal, and similar infections are given nearly as much attention as those due to staphylococci. The second half describes the measures that can be taken to control cross-infection. Almost every detail of hospital construction, management, and routine is discussed, from the ventilation of theatres to the operation of autoclaves, the choice of antibiotics, the washing of hands, and the value or otherwise of antiseptics.

One of the most valuable features of the book is the strictly judicial attitude—agnostic is the term they themselves use—which the authors have adopted. In consequence, they draw firm conclusions only when there is sufficient evidence to warrant them. Salutary as this is when discussing the epidemiology of infection, if only because it emphasizes how little is still known, it is even more so when they deal with the techniques required for its prevention. They accordingly hesitate to advocate the adoption of new measures or the substitution of an old technique by a new, unless it can clearly be shown that by so doing there will be a reduction in the incidence of infection. This ultra-conservative attitude may perhaps disappoint some, but there was certainly need for an impartial appraisal of techniques that can be used for the prevention of infection. It is for this reason, above all, that the book should be welcomed by anyone—bacteriologist, surgeon, nurse, or administrator—who has to deal with cross-infection. Its one fault is the index, which is, frankly, bad.

R. HARE.

NEUROCHEMISTRY OF EPILEPSY

Neurochemistry of Epilepsy: Seizure Mechanism and their Management. By Donald B. Tower, M.D., Ph.D. (Pp. 335 +x; illustrated. 72s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

The problem of epilepsy is a very serious one, for in the United States it is estimated that one person in every hundred is affected. Dr. D. B. Tower has therefore performed a great service in writing this relatively short monograph. After a brief historical survey—epilepsy was certainly known in Babylon—there are three chapters dealing with cerebral oxidative metabolism, with amino-acid metabolism, including vitamin B_6, and with electrolytes, such as sodium and potassium, and with transmitter substances such as acetylcholine. These three chapters are mainly devoted to biochemistry and to physiology, more especially of the neurone. Considerable importance is given to glucose metabolism and electron transport systems, reference also being made to electrically induced convulsions and to one pyridoxine-dependent patient. Amino-acid metabolism is discussed fully, with special emphasis on glutamate and γ-amino-butyric acid.

The chapter on electrolytes and transmitter substances is very interesting, and is a good synopsis of recent work. There is a discussion on the neurochemistry of conduction and transmission and the results found in cerebral activity. There is also a short discussion on the problem of the extracellular space in the brain, but no final conclusion is arrived at. Finally, there is a chapter on anticonvulsants followed by a short summary.

Dr. Tower is well known for his experimental approach to this problem of epilepsy, and he has quoted extensively from his work, more especially on asparagine and γ-amino-butyric acid, and has provided a well-balanced monograph with mainly a biochemical and physiological basis. Extremely few references are made to the E.E.G. or to patients, for this is essentially a scientific volume. Clinicians will find it hard to follow, but the scientist will profit greatly.

The volume is well produced, and has a good index of subjects as well as of authors. Very few errors were found. The line drawings are excellent and are understandable.

J. N. CUMINGS.

MEDICAL ILLUSTRATION

Illustrating Medicine and Surgery. By Margaret C. McLarty, D.A.(Edin.) With a Foreword by Sir Robert Macintosh, M.A., D.M., F.R.C.S.(Edin.), D.A. (Pp. 158+viii; illustrated. 37s. 6d.) Edinburgh and London: E. and S. Livingstone Ltd. 1960.

This book will be of great interest to art students and youngsters leaving school who are interested in the subject. The text is clear and simple, and contains many tips gained by years of experience. It is, though, confined entirely to the traditional type of medical book and journal illustration. For doctors and surgeons there is little new, and it does not cover at all comprehensively the role of work of the medical artist. Exhibits, models, and films, which nowadays can form the major part of an artist's work, are entirely omitted, as are the present trends and future advancement of medical illustration.

The author writes well and wisely within her self-imposed limits, but many of the illustrations are obvious padding, such as Figs. 20, 21, and 22, showing bottles of ink, while there are few really stimulating examples of medical illustration. In spite of appendices covering proof correction marks and conversion factors for weights and measures, the book is not comprehensive enough to be a reference or textbook for the young medical art student, or an illustration department.

SYLVIA TREADGOLD.

PROBLEMS OF ILLEGITIMACY

The Unmarried Mother and Her Child. By Virginia Wimperis, M.A.(Cantab.). Edited by Clifford Witting. (Pp. 397. 35s.) London: George Allen and Unwin Ltd. 1960.

Having outlined the extent of the problem and the sources of help available for mother and child, the author passes to a consideration of what happens to illegitimate children as they grow up—some in the grandparents' home, some adopted, some in the care of voluntary societies, some in public care. A formidable proportion of the children in long-term public care are illegitimate, partly because, unless adopted early in life, the child of an unmarried mother who is not cohabiting

steadily and who has not married often lacks the circle of affection and responsible relatives and friends that usually surround the luckier legitimate child, partly because so many illegitimate children are born into problem families. One group, tragic because they enter care so late, are those "beyond control." Many of the mothers who try to keep their children are so sorely lacking in the qualities needed—affection and responsibility, mental stability, health, and fair earning power—that probably they should have been advised at a very early stage to seek adoption rather than to try to bring up the children themselves. The final chapter poses the question, How can the illegitimate rate be reduced? In the past, society has relied to that end chiefly on deterrents. These have largely failed, though public opinion does help to limit the number of illegitimate births. Forced marriage is not the answer. Earlier marriages, legalized abortion, easier divorce, all have obvious disadvantages; nor does birth control provide a satisfactory solution. Over the years a happy home background is probably the factor most likely to solve the problem; meanwhile society must treat these mothers and children with humanity, seeking to resolve the tension between two needs—to safeguard society against irresponsible parents and to safeguard the child's future: "The danger is that the less one knows about illegitimacy, the more one tends to have strong feelings."

T. FERGUSON.

DENTAL ANAESTHESIA

General Anaesthesia for Dentistry. By James McNaught Inglis, M.B., Ch.B., F.F.A. R.C.S.(Eng.), D.A., and Victor Campkin, M.B., B.S., F.F.A. R.C.S.(Eng.), D.A. (Pp. 88+viii. 10s. 6d.) London: Edward Arnold (Publishers) Ltd. 1960.

Dental students and others interested in dental anaesthesia will find this a useful, straightforward account of current practice. The authors support, in general, the use of nitrous oxide for this type of surgery, though they do not hesitate to supplement it with more potent drugs when necessary. Their approach to the many difficult problems in dental anaesthesia is a balanced one; the views expressed represent a middle path, in a time of transition from the more classical methods of chairside general anaesthesia to ones involving newer agents and ideas. There are no illustrations, and, though details of technique are not lacking, the text is more suitable for revision or for the preparation of lectures than for the acquisition of the practical art of administering anaesthesia. Within these limitations the authors achieve their objective of a cheap, readable, concise, and up-to-date account of the present position of general anaesthesia for dentistry.

W. W. MUSHIN.

MENTAL HEALTH POLICY

Mental Health and Social Policy, 1845–1959. By Kathleen Jones, Ph.D. (Pp. 237. 28s.) London: Routledge and Kegan Paul. New York: The Humanities Press. 1960.

In her first book—*Lunacy Law and Conscience, 1744–1845*—Dr. Kathleen Jones described "the triumph of common sense and humanity," as Lord Ashley put it, which during the last half of the eighteenth century and the first half of the nineteenth led to the establishment of the county asylums and the heyday of the "moral treatment of the insane." In her new book Dr. Jones continues the story from the mid-nineteenth century to the present day, and tells how by the end of the century "common sense and humanity" had been almost defeated by "legalism" and how, in the present century, the wheel has again come full circle, culminating in the Mental Health Act of 1959, in which "common sense and humanity" are again to the fore. The Act is set in perspective against the preceding developments in scientific knowledge, psychiatric practice, and public attitudes which made such a law possible.

By this scholarly and readable book Dr. Jones consolidates her position as the social historian of psychiatry and mental illness. It should be read by all who treat the mentally ill or who are responsible for administering the services in which they are treated.

G. R. HARGREAVES.

SENSORY CHANGES FROM BRAIN WOUNDS

Somatosensory Changes after Penetrating Brain Wounds in Man. By Josephine Semmes, Sidney Weinstein, Lila Ghent, and Hans-Lukas Teuber. (Pp. 91+xiii; illustrated. 32s.) Cambridge, Mass.: Harvard University Press. London: Oxford University Press. 1960.

This is a disconcerting study of disturbed sensation in war veterans who have had penetrating brain wounds. There is a competent statistical analysis of the findings, but these are so contrary to usual neurological experience that one feels there must be some errors in the method. The most obvious criticism concerns the attempts made to define accurately the site of wounding, and particularly the claim to identify lesions which *spare* the sensori-motor region. Further, there is no indication whether the upper or lower part of the sensori-motor cortex was injured, while sensation was tested only on the palm and thumb of the hand. The choice of the palm of the hand for two-point discrimination is a poor substitute for the pulp of the fingers, and to leave out the lower limb and ulnar fingers in cases of upper parietal wound is unreasonable. Further, there is no record of the degree of associated motor disorder or the nature of focal fits, all of which would modify the clinical assessment of the findings. The most surprising finding was the high incidence of sensory loss in the hand ipsilateral to the side of wounding. This was usually associated with sensory loss in the contralateral hand—but not always. Further, there was a striking difference between the right and left hand in that ipsilateral changes were much more common in left-sided wounds. The reviewer finds it difficult to accept all of these findings on the information presented.

W. RITCHIE RUSSELL.

SURGICAL BANQUET

Current Surgical Management II. A Book of Alternative Viewpoints on Controversial Surgical Problems. Edited by John H. Mulholland, M.D., Edwin H. Ellison, M.D., and Stanley R. Friesen, M.D. With 50 contributors. (Pp. 348+xxi; illustrated. 56s.) Philadelphia and London: W. B. Saunders Company. 1960.

The editors of this unconventional volume justly claim that it presents differing viewpoints on certain controversial surgical topics. Read separately, the majority of the individual chapters seem to be authoritative until other relevant contributions are studied. Then the reader is reminded that "there may be more than one way to skin a rabbit." The differences, however, are usually shades rather than clashes of opinion. The unorthodox arrangement of the sections in the book is said to reflect the magnitude of the problems which arise in general

surgery: the unusual form is not a detraction, although some readers will, no doubt, conclude that the degrees of magnitude of their own individual surgical problems are not so specific.

Fifty contributors provide 38 articles: there are four articles on duodenal ulcer and its complications, three on polyps of the colon, three on repair of oesophageal hiatal hernia, two on the choice of operation for carcinoma of the head of the pancreas, two on the detection of common duct stones, two on the management of the common duct wound, two on the repair of common duct stricture, two on the management of the normal gall-bladder at sphincterotomy, two on the pathogenesis and management of pilonidal sinus, one on carcinoma of the breast, two on the management of small bowel obstruction, four on the management of arterial insufficiency of the lower extremities, two on thrombo-embolism, three on acute renal failure, two on pre-operative preparation of the colon, and two on prolapse of the rectum.

It would be invidious to single out for praise any particular article: all are good, clearly written, and well edited. There should be a large demand for this book; though the inexperienced may find it causes some degree of mental indigestion, the well-trained critical surgeon should take this surgical banquet in his stride and ask for more.

R. SHACKMAN.

STUDY OF GOUT

La Goutte. By S. de Sèze and A. Rickewaert, with the assistance of J. Levernieux and R. Marteau. (Pp. 268; illustrated. NF. 47.) Paris: L'Expansion Scientifique Française. 1960.

This is a complete study of gout. The book begins with an interesting historical view of the subject. The rest of the work is devoted mainly to progress which has been made in the knowledge of gout over the last 50 years or so. These advances are compared and contrasted with classical views.

The views expressed in the clinical and therapeutic sections are based on a careful study of 180 cases of gout under the care of the authors. The conclusions drawn are not merely expressions of opinion but are based on an analysis of their findings, which are compared with other contemporary series. All the cases showed at least one of these diagnostic criteria—typical acute attacks affecting the big toe, arthritis sensitive to colchicine, or the presence of tophi. The sections of morbid anatomy and pathogenesis are based on largely published works of other authors. In line with modern views, the authors reject the existence of "visceral gout" and the gouty diathesis. They find that renal calculi, impairment of renal function, and possibly hypertension are the only conditions more frequently seen in their gouty patients than in a control series of patients of a comparable age.

The chapter on treatment is particularly valuable. The authors find phenylbutazone superior to colchicine for relieving the acute attack. They employ a rather higher dose than most physicians in Great Britain would recommend, with the result that the incidence of toxic effects tends to be considerably higher than is the general experience here. As a result they still use colchicine as the first choice. Like most other authorities they are now tending to use uricosuric agents earlier in the management of gout, though they formerly reserved these agents for patients with tophi or painful chronic gouty arthritis.

In spite of the recent advances in the drug therapy of gout, the authors still recommend a dietary regime for all cases, and cite evidence that acute attacks were less frequent among their patients during the war rationing period. This book is well printed, easy to read, and can be recommended to anyone with an interest in gout.

V. L. STEINBERG.

PAEDIATRIC DERMATOLOGY

Pediatric Dermatology. By Henry H. Perlman, M.D., Phar.D. (Pp. 477+xii; illustrated. £6 15s.) Chicago: Year Book Publishers, Inc. London: Interscience Publishers, Ltd. 1960.

Dr. Perlman has written an excellent textbook on skin disease in childhood, which is comprehensive and of reasonable length. The need for such a book in English has been felt for a long time, though the first English textbook devoted to paediatric dermatology appeared so long ago as 1827, when Walter Dendy published his *Cutaneous Diseases Incident to Childhood.* All those who have to deal with children, from the young resident or student to the more experienced paediatrician, will find it a valuable guide. The general practitioner will welcome it, and he will be particularly grateful for the well-chosen and excellently produced photographs, which will often help him to diagnose the more difficult and rarer case.

The author has given us a well-balanced work, obviously based on long experience of skin diseases in children. His views are orthodox, although, naturally enough, there are many differences in treatment and management, mainly minor, which reflect American rather than British practice. A major difference is in the management of the very common strawberry marks, which most British dermatologists would allow to disappear spontaneously, rather than interfere with them by surgery, radiotherapy, or freezing. The chapter on the newborn is perhaps too short and should be expanded in the next edition, as skin disease at this age can often present considerable diagnostic difficulties. The chapters on eczemas, tuberculosis, the fungous diseases, and the zoonoses are very good indeed, but congenital anomalies will require more thorough treatment in future editions, as their relative importance increases. Phenylketonuria is not indexed; the relatively high frequency of eczema in this condition, and the fact that eczema may be the presenting symptom in the earliest weeks of the disease, are not as widely known as they should be. Nevertheless Dr. Perlman has kept the balance of his book remarkably well, and he gives due emphasis to the commoner and more serious disorders. We may be sure that further editions will be called for and these minor defects will be dealt with. The book can be recommended unhesitatingly, and the publishers can be pleased with an excellent production.

E. J. MOYNAHAN.

MENTAL RETARDATION

Mental Retardation. Proceedings of the First International Medical Conference at Portland, Maine. Edited by Peter W. Bowman, M.D., and Hans V. Mautner, M.D. (Pp. 530+xiv; illustrated. $12.50.) New York and London: Grune and Stratton, Inc. 1960.

For some years organized bodies of parents in Great Britain and the United States have sought to draw attention to the problem of mental retardation. The conference held at Portland, Maine, in 1959 is a measure of the success of their efforts. Several local associations

of parents were among the sponsors of the conference. This report of the proceedings is essential for anyone interested in recent advances in this rapidly developing subject. The emphasis in the contributions is on the scientific and aetiological aspects. Though inevitably in such a symposium the quality of the chapters varies, the general level is high. Among the British contributors is Professor Cumings, who writes on copper, iron, and lead in relation to the brain, whilst Professor Polani summarizes recent findings on chromosome anomalies in relation to mental subnormality, in particular in Klinefelter's and Turner's syndrome and in mongolism.

One of the most important of recent developments in the understanding of malfunction and maldevelopment of the brain is lucidly discussed by D. Y.-Y. Hsia under the head of "Enzyme and Mental Deficiency." He mentions 13 "inborn errors of metabolism" which give rise to mental defect, pointing out that this branch of knowledge is still in its infancy and suggesting that in 10 or 20 years a whole conference will be required to do justice to the subject. Illustrating possible therapeutic developments, he hopes that "more effective means at an enzyme and metabolic level" may be used to prevent brain damage from hyperbilirubinaemia instead of the present tedious technique of exchange transfusion. Wortis and Jackson were unable to identify the presumed toxic substance in the serum of phenylketonurics, but found that this serum caused a reduction in the oxygen uptake of rat-brain tissue. The value of the volume for reference would have been enhanced by an author index.

B. KIRMAN.

BOOKS RECEIVED

Review is not precluded by notice here of books recently received.

The Catarrhal Child. By John Fry, M.D.(Lond.), F.R.C.S. (Eng.). (Pp. 139+viii. 25s.) London: Butterworths. 1961.

Ciba Foundation Study Group No. 6. ***Metabolic Effects of Adrenal Hormones in Honour of Professor G. W. Thorn.*** Editors for the Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B., M.R.C.P., and Maeve O'Connor. (Pp. 109 +viii; illustrated. 12s. 6d.) London: J. and A. Churchill Ltd. 1960.

Adrenergic Mechanisms. Ciba Foundation Symposium jointly with Committee for Symposia on Drug Action. Editor for the British Pharmacological Society: J. R. Vane, B.Sc., D.Phil. Editors for the Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B., M.R.C.P., and Maeve O'Connor, B.A. (Pp. 632+ xx; illustrated. 70s.) London: J. and A. Churchill Ltd. 1960.

The Cutaneous Manifestations of the Benign Inflammatory Reticuloses. Edited by Samuel M. Bluefarb, B.S. M.D., F.A.C.P. (Pp. 408+xviii; illustrated. £5 12s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

The Chemical Basis of Clinical Psychiatry. By A. Hoffer, M.D., and Humphry Osmond, M.R.C.S., D.P.M. (Pp. 277+xvi. 68s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

The Chemistry of Immunity in Health and Disease. By David W. Talmage, M.D., and John R. Cann, Ph.D. (Pp. 178+ xi; illustrated. 46s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1961.

Medical Forms and Procedures for Industry. By Herbert L. Herschensohn, M.D. (Pp. 192+xv. 68s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1961.

Micro-Organisms as Allies. The Industrial Use of Fungi and Bacteria. By C. L. Duddington. (Pp. 256; illustrated. 25s.) London: Faber and Faber. 1961.

Eating Your Way to Health. The Bircher-Benner Approach to Nutrition, with a Complete Cookery Book. By Ruth Bircher. Translated and edited by Claire Loewenfeld. (Pp. 372. 30s.) London: Faber and Faber. 1961.

Parasitology (Protozoology and Helminthology) in Relation to Clinical Medicine. By K. D. Chatterjee, M.D.(Calcutta). (Pp. 192; illustrated. Rs. 18.75.) Calcutta: S. N. Guha Ray, Sree Saraswaty Press Ltd. 1960.

Evaluation and Management of the Brain-Damaged Patient. By Jerome S. Tobis, M.D., and Milton Lowenthal, M.D. (Pp. 109 +xii; illustrated. 48s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

The Tutoring of Brain-Injured Mentally Retarded Children. By James J. Gallagher, Ph.D. With a Foreword by Samuel A. Kirk, Ph.D. (Pp. 194+xv. 54s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1961.

Cleft Lip and Palate Rehabilitation. By William H. Olin, D.D.S., M.S. With a Chapter by Duane C. Spriestersbach, Ph.D. (Pp. 194+ix; illustrated. 72s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1961.

Quantitative Cellular Haematology. By J. M. Yoffey, D.Sc., M.D., F.R.C.S.(Eng.). (Pp. 122+xv; illustrated. 44s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1961.

Speech Therapy in Cerebral Palsy. By Merlin J. Mecham, Ph.D., Martin J. Berko, M.A., and Francis Giden Berko, M.A. (Pp. 307+xi. 80s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

The Pathology of Cerebral Palsy. By Abraham Towbin, M.D. (Pp. 206+xi; illustrated. 64s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Textbook of Medical Physiology. By Arthur C. Guyton, M.D. Second edition. (Pp. 1,181+xxvi; illustrated. £5 8s.) Philadelphia and London: W. B. Saunders Company. 1961.

Atlas of Anatomy and Surgical Approaches in Orthopaedic Surgery—Lower Extremity. By Rodolfo Cosentino, M.D. With a preface by Carroll B. Larson, M.D. (Pp. 263; illustrated. £5 12s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Parkinsonism. Its Medical and Surgical Therapy. By Irving S. Cooper, M.D., Ph.D., F.A.C.S. (Pp. 239+xii; illustrated. £6 18s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1961.

The Story of Hospital Almoners. The Birth of a Profession. By E. Moberly Bell, with a foreword by Sir Ernest Rock Carling, F.R.C.S., F.R.C.P. (Pp. 160; illustrated. 13s. 6d.) London: Faber and Faber. 1961.

The Control of Disease in the Tropics. A Handbook for Medical Practitioners. By T. H. Davey and W. P. H. Lightbody. Second edition. (Pp. 422+xii; illustrated. 47s. 6d.) London: H. K. Lewis and Co. Ltd. 1961.

The Transplantation of Tissues and Organs. By Michael F. A. Woodruff, M.D., M.S.(Melb.), F.R.C.S., F.R.C.S.E., F.R.A.C.S. (Pp. 777+xxxiii; illustrated. £10 4s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

The Surgical Treatment of Portal Hypertension Bleeding Esophageal Varices and Ascites. By M. Judson Mackby, M.D., D.A.B.S., F.I.C.S. With a foreword by Emile Holman, M.D. (Pp. 250+xviii; illustrated. 84s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Hearing Enhancement. By John A. Victoreen, LL.D., with a foreword by Frank S. Forman, M.D. (Pp. 183+xiv; illustrated. 60s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1960.

Experiencias Sobre Enfermedades Tropicales en Zonas Rurales de Venezuela. By Luis Dao. (Pp. 397+vii; illustrated. No price.) Caracas, Venezuela: Corporación Universo Ltda. 1960.

The Medical Directory of South Africa 1960. (Pp. 360. No price.) Durban: The Knox Publishing Co. 1961.

Toxicity of Industrial Metals. By Ethel Browning, M.D. (Pp. 325+vii+14. 50s.) London: Butterworths. 1961.

Médecine Sociale de l'Adolescent. Sa Mise au Travail. By Louis Christiaens. Preface by Professeur Julien Marie. (Pp. 613. N.F. 54.) Paris: G. Doin et Cie. 1960.

Notes on W.V.S. Health and Hospital Work. (Pp. 43. No price.) London: W.V.S. Headquarters, 41 Tothill Street, S.W.1. 1960.

The Thing Called Space. By Jay E. Darlington. (Pp. 96+ ii. $2.) Chicago, Illinois: Parkway Press. 1961.

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THE MODERN DOOMSDAY

On April 23 the population of Great Britain will receive the decennial invitation to count themselves. The national census which has taken place at intervals of ten years since 1801 (except for the distracted year of 1941) will once more be upon us. Almost everything that is done by the people for the people entails numbering the people, and this regular stocktaking is an essential part of good national housekeeping, including the efficient running of the health services. All this is clearly set out in a booklet just produced by the General Register Office and the Central Office of Information.[1]

Owing to the growing need for social statistics of various kinds, the full range of questions in the 1961 household schedule will be a little greater than in 1951. There are some additions on housing; new questions have been introduced on the type of building (single or multi-dwelling, wholly or partly residential), type of tenure (owner-occupied, rented), and on hot-water supply. The 1951 questions on rooms, water-closets, and baths are repeated. A few more questions than in 1951 are being asked on marriage and size of family (number of live-born children) in order to improve estimates of fertility—the main element in forecasting the population. An important addition, which will provide valuable information for town planners and housing authorities and for those engaged in the difficult task of making local population estimates, is a question about change of usual address within the year preceding the census date, supplemented by a question about the length of stay at the same address of the non-movers. This will enable the main streams of internal migration to be identified. At present this vast ebb and flow of population goes unrecorded. Apart from showing where the migrants are concentrated geographically, it will also show what sort of housing they seek, the size of their families, the occupation and industry affiliations of their occupied members, and the age composition of the households. There is a new section on the schedule to establish the usual composition of households as distinct from what it happens to be on census night.

Finally, additional sharpness has been introduced in the recording of details of occupation. There has been much interest in the care of the elderly worker, and especially in the possibility of providing him with suitable part-time employment. Therefore, male part-time workers will be asked to indicate their previous whole-time occupation, and all part-time workers are to be asked how many hours they work. Against a background of a shortage of scientists of all kinds in industry and in research institutions an attempt will be made to obtain information on the numbers of scientists and where they are working. Medical, dental, and optical qualifications are excluded because sufficient information is already available from the professional directories.

The most important innovation in the 1961 census is the use of sampling in the field to reduce the burden on the public, for the full range of questions will not be asked of all households but only one in ten. The remaining nine-tenths will have to answer only a few questions which are either basic, such as age, sex, marital condition, or are about subjects on which a sample would not provide sufficient data, such as birthplace and fertility. They will, in fact, have fewer questions than their predecessors have had to answer in any census in this century. The choice of one-tenth as the sampling fraction is based on a proper assessment of data requirements. The figure is a compromise; for some questions it will be a little in excess of minimum needs and for others it will be barely sufficient. The sample will be designed to ensure that it is random and fully representative. The 80,000 enumeration districts into which Great Britain is divided for purposes of the enumeration will be listed systematically, and a random number between one and ten taken serially from a table will be allocated to each district. If this number is, say, 4 the enumerator will give a sample schedule to the 4th, 14th, 24th, etc., household in order. The arrangement is covered by the Census Regulations and will be legally enforceable; it will be strictly followed by the enumerator. In practice the sample and non-sample schedules will be interleaved in the required order before they reach the enumerator, who will simply distribute them by taking them one by one off the top of the pack as he goes from household to household. The allocation will be made by the General Register Office without any prior knowledge of which households may be involved, and the enumerator will be acting automatically without any personal control over the allocation. In hospitals and

[1] *Why a Census?* General Register Office and Central Office of Information. H.M.S.O. Price 1s.

other institutions the sample will be one of persons, not households.

In order to speed up the production of the tables and thus render unnecessary the advance 1% tables such as were produced for the 1951 census, automatic data processing methods are to be used. The General Register Office has access to the large modern electronic computer installed near Winchester for the Royal Army Pay Corps. But the speed-up will not be dramatic, because, though the actual tabulations are completed in a small fraction of the time taken by orthodox punched card machines, the computer (which is far from being the popularly conceived "brain") will need thorough prior instruction (programming) and this takes considerable time and skill. A great advantage of such processing of the data is the ability to detect rapidly any inconsistencies in them. The computer can be instructed to make an internal scrutiny of the input and to "clean it up" before tabulations are produced. In some cases the computer will indicate the record as being one which must be checked back to the actual schedule, in others it will automatically make a prescribed adjustment. Another advantage of the computer will be the compact storage of the data on magnetic tape, thus rendering it more accessible for supplemental tabulations for research purposes when the main tabulations are completed. Publication, too, will be speeded. The results from the computer will be printed out on an electric typewriter in final form for photographic reproduction.

The traditional features of the British census remain: self-enumeration by the householder (the enumerator so-called merely delivers and collects the schedules), and strict confidentiality, strongly safeguarded. This is a great exercise in public collaboration. Medical practitioners, who treat their patients better because they see them both as individuals and as parts of a larger social complex, have an ultimate interest in the success of the operation and will wish it well.

CHRONIC HEADACHE

Headache must surely be one of the commonest symptoms to bring a patient to his doctor. Several paroxysmal headache syndromes have been gradually recognized and defined. Migraine, for instance, which is probably the commonest of all recurrent headaches, has been defined as being a paroxysmal unilateral headache, preceded by visual or sensory phenomena and followed by prostration and by nausea or vomiting or both. This definition may be satisfactory for a typical case, but it must be accepted that the headache is often bilateral, that the aura may be absent or may even occur without the headache, that attacks vary considerably in severity, and that the paroxysmal occurrence of the headache is its most characteristic quality. In common with the great majority of organically determined headaches, that of migraine is often present on waking or begins in the mornings, and, like that resulting from raised intracranial pressure due to intracranial tumour, it is commonly accentuated by stooping, by coughing, or by sudden changes in posture. The same is of course true of the headache, presumably of vascular origin, which sometimes follows influenza or other debilitating illnesses, and which is similar to that of the alcoholic hangover. Another syndrome recently defined is the "cough headache,"[1] in which the patient experiences a severe though transient headache, brought on by a bout of coughing and sometimes by straining or sneezing. Though some of these patients are eventually found to have an intracranial lesion causing increased pressure, there are many more in whom the syndrome is essentially benign, though tending to recur over the years. Periodic migrainous neuralgia, as originally described by Wilfred Harris,[1] is yet another syndrome with stereotyped clinical features, which have been well documented by Sir Charles Symonds[2 3] and E. R. Bickerstaff.[4] In this condition the patient experiences attacks of severe burning pain in, around, or behind one eye; the attacks usually last for between thirty minutes and two hours and occur in bouts, often of several weeks' duration, during which one to three attacks occur in each twenty-four hours, often consistently at the same time of the day or night. This syndrome probably embraces many cases previously diagnosed as examples of so-called histamine headache, ciliary neuralgia, sphenopalatine or vidian neuralgia (vidian from Guido Guidi, lat. Vidius, 1500–69), and many more. Its recognition is important, because bouts can often be aborted by prophylactic ergotamine therapy. The condition differs in its clinical features from the sharp momentary lancinating attacks of pain, triggered by speaking, by chewing or by touching the face, which occur in true trigeminal neuralgia, and also from the dull continuous ache in the upper jaw which is common in middle-aged women—the so-called atypical facial neuralgia which is usually due to or associated with depression, tension, or other emotional disturbances.

Clearly there are many other causes of organic headache which can sometimes appear to be

[1] Harris, W., *Neuritis and Neuralgia*, 1926. London.
[2] Symonds, C., *Brain*, 1956, **79**, 557.
[3] —— ibid., 1956, **79**, 217.
[4] Bickerstaff, E. R. *Lancet*, 1959, **1**, 1069.
[5] Braaf, M. M., and Rosner, S., *N.Y. State J. Med.*, 1960, **60**, 3987.
[6] Campbell, A. M. G., and Lloyd, J. K., *Lancet*, 1954, **2**, 1034.

paroxysmal; among these dental sepsis and sinusitis are prominent, but in such cases local pain and tenderness will generally lead to the correct diagnosis. Furthermore, though many physicians are sceptical of the importance of "eyestrain" in the aetiology of headache, it seems that the increased tension in the periorbital muscles which may be unconsciously induced in an attempt to overcome a refractive error can be an important cause of frontal headaches and that these are generally cured by the provision of spectacles. Temporal or cranial arteritis is another cause of headache which must be borne in mind, particularly in the elderly. In these cases the scalp is often sore and tender, the temporal arteries show undue tortuosity or diminished pulsation, and the patient feels general malaise; the erythrocyte sedimentation rate is always raised, and there is an ever-present risk of blindness due to retinal-artery occlusion, which is greatly reduced by steroid therapy.

Much more difficult, from the diagnostic point of view, however, are the very large proportion of cases of chronic headache in which the clinical picture suggests none of these clearly defined clinical entities. In many such cases the headache is present daily, is continuous though of variable severity, frequently becomes worse towards evening, is frontal or occipital in distribution, but is not associated with visual symptoms or with nausea or vomiting. In a recent study of 2,000 such cases, observed over a 14-year period, M. M. Braaf and S. Rosner[5] have concluded that degenerative changes in the cervical spine, both in the intervertebral disks and in the joints of the spine, with consequent compression of cervical nerve roots, were the factors responsible for the patient's symptoms in over 90% of cases. They noted that there had been frequent or severe trauma to the neck in many of their patients, and believed this factor to be of considerable importance. They claimed that the patients received substantial benefit from cervical traction in the great majority of cases. Unfortunately the evidence presented is hardly a sufficient basis for these conclusions. The syndrome was seen twice as often in females as in males, in whom cervical spondylosis is much more common, and the authors described a wide variety of emotional symptoms, including disorders of mood, of concentration, and of memory, severe fatigue, flushing, and lack of energy, which were regarded as an integral part of the syndrome. Indeed "general irritability" was invariable. It cannot be denied that cervical spondylosis may cause occipital headache, but it seems much more probable that the headaches and associated symptoms described in this series of cases were essentially psychogenic and that the underlying illness was in some cases endogenous depression, in others chronic tension and anxiety.

It must surely be the experience of every neurologist that most patients whose headaches do not fall into any of the categories described above, and who are not suffering from organic intracranial disease, have signs and symptoms, which may not at first be overt, of emotional disturbance. Sometimes the headache is worse when the patient is tired (in the evenings), when tension is at its height, or even when it has relaxed (at the week-ends). It is of course important to recall that depression and anxiety may result from or coexist with organic intracranial disease. But many patients with chronic unexplained headache will respond to treatment along traditional lines from their family doctor while others require thymoleptic and/or tranquillizing remedies. Cervical traction in the cases described by Braaf and Rosner[5] probably had a non-specific effect; the same may have been the explanation for the relief of atypical facial neuralgia, a somewhat similar condition, which was achieved by immobilization of the cervical spine in some of the cases described by A. G. M. Campbell and J. K. Lloyd.[6]

VENTILATION OF OPERATING-THEATRES

Despite earlier disbelief, it is now accepted that airborne bacteria may enter wounds at the time of operation and that sepsis may result. This is most likely to happen when the operating-theatre is ventilated by exhaust. Many old theatres have a single extraction fan installed to suck out steam and anaesthetic gases. The air the fan extracts has to be replaced, and it usually comes into the theatre through doorways from other parts of the hospital. If the theatre is in an isolated block this may not matter, but ventilation of this sort may become dangerous if the theatre is connected to the main source of staphylococci, the hospital ward.

To minimize the chances of infection the first duty of the ventilation engineer is to provide the theatre with plenum or positive-pressure ventilation. With such a system clean filtered air is blown into the theatre at such a rate that air is always moving out from the theatre to other parts of the hospital, and never in the reverse direction. The engineer's second task is to arrange the airflow in the theatre so that bacteria liberated from carriers in the surgical team or from the patient may be removed as quickly as possible. There are two rather different ways of

[1] Blowers, R., and Crew, B., *J. Hyg. (Lond.)*, 1960, **58**, 427.
[2] Lidwell, O. M., and Williams, R. E. O., ibid., 1960, **58**, 449.

doing this. If the air is blown in from the side of the theatre, turbulent mixing of the air will take place. The alternative is to introduce air through perforations in the ceiling or through diffusers in the ceiling in an attempt to produce a downward piston of air and so sweep bacteria away to outlets at the sides. It is not yet possible to say which method is better. Not enough is known about the shedding of bacteria by carriers, and neither type of ventilation has been tested sufficiently in working conditions.

Meanwhile, now that new hospitals are being built and existing hospitals are being altered, recent papers by R. Blowers and Beryl Crew[1] and by O. M. Lidwell and R. E. O. Williams[2] are timely. Blowers and Crew report the results of a field study of twenty-two theatre suites, and the results of important experimental work in a full-sized model theatre. Lidwell and Williams, using a different technique, tested twenty-six theatres, all but two of which were provided with mechanical ventilation. Taken together these papers provide a wealth of information for anyone concerned with the ventilation of the operating-theatres.

It is disturbing, for instance, to find how often theatres which are nominally provided with positive-pressure ventilation draw air in from the hospital under some conditions. The usual reason for this accident is that, owing to too much air being extracted from the theatre, too little of the surplus of input over extract is left to pressurize doors. Air extraction is needed to remove heat and steam or to provide balanced conditions, but it is doubtful if it is required in the theatre itself, and there is much to be said for the hinged and weighted flap on the theatre door advocated by Blowers and Crew. Fortunately air movements can be observed very easily by watching plumes of titanium tetrachloride smoke, and a surgeon who wants to know if his theatre is pressurized can test it very simply himself. It is not easy to determine the speed at which bacteria are removed from a theatre, and for detailed reference to this and for much information relevant to the ventilation of the operating-theatre the reader is referred to the papers.

Ventilation is necessary for other reasons, notably for the comfort and safety of the patient and the staff. Fortunately during most of the year in Great Britain ventilation which is bacteriologically safe will also provide comfortable working conditions. On hot and humid days cooling may be required, but there is some dispute about whether the provision of cooling equipment is economically justified. Until the dispute is settled, much more can be done to suppress the release of "wild" heat in the theatre. Unlagged sterilizers and steam pipes or fundamental defects such as the inclusion of steam pipes in the same channel as the air duct, all raise the temperature of the air. Instrument autoclaves in the theatre suite are potential sources of much unnecessary heat. Every attempt should be made to lag these instruments and the large control panels that go with them as effectively as possible. Many theatres could be made more comfortable, and at low cost, by the suppression of unnecessary heat at source.

"UNSUITABLE FOR EDUCATION AT SCHOOL"

A consequence of the coming into force of the Mental Health Act, 1959, has been the introduction of new arrangements to deal with children whose disability of mind makes them unsuitable for education at school. The appropriate section in the Education Act has been replaced by new provisions in the Mental Health Act. The children are no longer classified as mentally defective and declared to be ineducable but are to be recorded as unsuitable for education at school. The difficulties remain, but the defeatist attitude has been abolished. The new provisions, which extend the rights of parents, alter the legal procedure, and simplify some of the administrative arrangements, are described in a recent circular[1] issued by the Ministry of Education.

Briefly, it is the Ministry's hope that the small number of children capable of profiting from education but not suitable for ordinary or special schools should not be officially excluded from school but considered for "special educational treatment" on the lines of that available for maladjusted children. The larger group of severely subnormal children, who cannot benefit even from such special education as the authority can provide, may be recommended for training in training centres of the local health authority or in hospital. The local health authority is empowered to compel attendance at training centres of children recorded by the local education authority as unsuitable for education at school, but, apart from this power, it can also give help and guidance on a purely voluntary basis.

The local education authority can require a parent to submit any child who has attained the age of 2 years for medical examination. The circular suggests that an informal and friendly letter setting out the authority's intentions and the parents' rights should accompany the formal notice, and it recommends a personal approach by an officer of the authority who can discuss the forthcoming medical examination and answer the parents' questions. The doctor examining the child can also give the parents useful advice about his future care and training.

It is hoped that an increasing proportion of mentally handicapped children will have had an opportunity of

[1] Ministry of Education Circular 12/60.

receiving special educational treatment before being formally examined. Delay in making a decision until the child reaches school age may well be in the child's interest. By that age many children will have had their future care settled by mutual arrangement between parents and the local health authority. It has long been the practice to give every child a trial period at school, or special school, if they are not obviously unsuitable. But the Ministry of Education's circular suggests this period should not be too long, for delay may not be in the child's or the school's interest, and parents may develop false hopes about the capabilities of the child.

Children who leave school and are, in the opinion of the local education authority, in need of care and guidance because of mental handicap will continue to receive this from the local health authority, not by statutory report as previously but by informal passage of information between the two authorities. Here again personal explanation by the field workers to the parents should remove misunderstanding. The whole tenor of the new arrangements is conducive to an atmosphere of reasonableness. The elaborate and cumbersome methods of the past, although still necessary in a number of cases, have been put into the background and a more natural and informal relationship fostered between parents and the education authority.

ALCOHOL AND DRIVING

In 1960 in Great Britain nearly 7,000 people died as a result of road accidents and over 80,000 were seriously injured. The determination of the present Minister of Transport to do something to reduce these shocking figures in future commands respect everywhere, and the Government last week introduced its Road Traffic Bill[1] to promote greater safety on the roads. Its first two clauses are concerned with drink and drugs, and the second clause in particular introduces the question of measuring the amount of such substances in the body. Clause 2 (1) says, first, that the court shall have regard to evidence on the "proportion or quantity of alcohol or of any drug" in the blood or "water" (i.e., urine) or breath of the accused person. Secondly, it says that refusal to provide a specimen for analysis may (unless a reasonable cause is shown) be treated as supporting evidence given by the prosecution or as rebutting evidence given by the defence.

Many people would agree that the unwise consumption of alcohol, by both pedestrians and drivers, is an important cause of road accidents. The police believe that it is a commoner cause than the statistics show, and the special committee of the B.M.A. concluded in its report,[2] published last year, that the official returns underestimate "very considerably" the number of accidents due to this cause. J. Cohen and colleagues[3] and G. C. Drew and colleagues[4] showed that a smaller quantity of alcohol than was generally known—or at least generally admitted—could impair a person's skill at driving or at carrying out a test. But it is one thing to test the effects of alcohol on a series of volunteers, another to interpret the data justly when a person's liberty is at stake. The attempt is made every day in the courts, and this Bill may well provide the means of doing it with greater precision.

[1] Summarized at p. 973.
[2] Report of a Special Committee of the British Medical Association, *Relation of Alcohol to Road Accidents*, 1960.
[3] Cohen, J., Dearnaley, E. J., and Hansel, C. E. M., *Brit. med. J.*, 1958, 1, 1438.
[4] Drew, G. C., Colquhoun, W. P., and Long, H. A., ibid., 1958, 2, 993.

THE LONG AND THE SHORT OF IT

In an increasingly crowded world there might be some advantage in having a longer neck than other people. Can it be done? Ever since travellers first brought back their tales of "giraffe-necked" women in the Orient there has been speculation on the physiological mechanisms by which these people elongated their necks. Mr. R. Roaf,[1] of the Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry, has now investigated the matter, and unfortunately has had to head his report "A Myth Exploded." The women who are subjected to this strange mutilation belong to the Padaung tribe of East Burma. As is well known, coils of wire are applied to their necks. Mr. Roaf reports that on the first occasion, when the girl is 8–10 years old, a spiral of about ten coils is wound on. The wire is nearly half an inch (1.2 cm.) thick. Two or three coils a year are added until there are seventeen or eighteen round the neck. The result is certainly to make the neck look much elongated, but *x*-ray studies show that the appearance is due to "depression of the shoulder girdle and moulding of the upper ribs, as a result of which the superior portion of the thorax is compressed and elongated and is, so to speak, incorporated into the neck." Thus there is no true lengthening, and "the Padaung tribe are no more successful than modern orthopaedic surgeons in their efforts to produce overgrowth of bone." Mr. Roaf also records the interesting fact that all women who have had these coils applied develop high blood-pressure and usually die young from a cerebral stroke.

SYNOVIAL TUMOURS

Tumours of synovial tissues have always been a puzzle both to pathologists and to clinicians. Synovial membranes are a specialized form of connective tissue, and it might be expected that the tumours derived from these structures would be either fibromas (if benign) or sarcomas (if malignant). In essence this is true, but the histopathologist meets with difficulties because of the peculiar forms of differentiation of synovial tumours. The benign varieties of synovioma are generally fibrous in character, but they may also contain peculiar giant cells, myxomatous areas, and a variable number of synovial clefts. These benign tumours are mostly slow-growing and non-invasive and may readily be cured by

[1] Roaf, R., *J. Bone Jt Surg.*, 1961, 43B, 114.

simple local excision. In the past their interpretation has been bedevilled by confused nomenclature. They have been variously designated as "giant cell tumours of tendon sheaths," "myeloid tumours," "xanthomas," "endotheliomas," and "teno-synoviomas." If they had always been referred to as "benign synoviomas," both treatment and prognosis would have been more obvious.

The malignant synovial tumours are fortunately much rarer. The difficulties here derive partly from the rarity of the lesion, so that the experience of the individual pathologist is necessarily limited, partly from the complexity of the histology of the tumours, but mainly from the simple fact that the natural course of this variety of sarcoma is even more unpredictable than that of others. This is brought to light whenever a series of cases is collected and studied as a group. Recently R. G. Vincent[1] has reported on twelve cases of which he made a special histological study. His experience, which confirms that of other workers, is that malignant synoviomas (or synovial sarcomas) often grow very slowly at first, producing few symptoms. Then, suddenly, a tumour which has been quiescent enters a stage of active proliferation and metastasizes rapidly. When this stage has been reached there is little or no hope of cure by surgery, though *x*-ray therapy may be of some help. The best results are obtained when a tumour is correctly diagnosed at an early stage of development and promptly treated by radical surgery.

AT HOME IN HOSPITAL

Patients lying in hospital beds and nurses looking after them should both benefit from the publication by the Ministry of Health this week of a report which is surprisingly, and refreshingly, iconoclastic. Prepared by a committee of nurses under the chairmanship of Miss M. B. Powell, matron of St. George's Hospital, the report[2] bears the unexciting title of "The Pattern of the In-patient's Day," but contains some explosive suggestions—including the recommendation that the matutinal distribution of bed-pans and hand basins should be eliminated except for seriously ill patients. One table lists the traditional events of the in-patient day. The report comments:

> "It is apparent from the most cursory glance at this table that the patient is subjected to constant activity from the time he is awakened at 5 a.m. to 6 a.m. onwards, and that, even though in some wards the tempo of activity may drop a little in the second half of the day, in many wards it is constant until lights out at 10 p.m. . . . The major obstacle to be overcome seems to be the tendency for ward routine to be relatively inflexible."

This inflexibility not only annoys patients, it also puts unnecessary burdens on the nurses.

All the evidence the committee received confirmed it in its opinion that much of the present ward routine is dictated by the traditionally honoured belief that wards and patients must be prepared for a meticulous inspection by nine o'clock every morning. This leads to an unbalanced and inefficient use of staff. The committee therefore suggests that continuation of the practice of early-morning bed-making is unnecessary and could be drastically curtailed. With less routine bed-making and sanitary rounds abandoned, patients need not be wakened so early, and "there is no justification for waking the entire ward for, so to speak, a ceremonial cup of tea."

The report questions the need for the routine taking and recording of temperatures and pulse and respiration rates, and recommends that general ward cleaning should be postponed from just before dressings are usually done to later in the day. The committee even wonders whether it is really necessary for all activity to cease in wards during medical rounds, and boldly suggests that bed baths could perhaps be given at one end of a ward while a consultant was doing his round at the other.

This report will certainly give matrons something to think about. It deserves careful study, for its purpose is not only to relieve the relentless pressure on ward staff but also to allow patients to sleep longer and "to enjoy a day more nearly in accordance with that to which they are accustomed in their own homes."

[1] Vincent, R. G., *Ann. Surg.*, 1960, **152**, 777.
[2] Ministry of Health—Central Health Services Council, *The Pattern of the In-patient's Day*, 1961. H.M.S.O., London. Price 2s. net.

"FAMILY DOCTOR"

Ten years ago, on the first appearance of the B.M.A.'s popular health magazine, *Family Doctor*, we reminded our readers that the Representative Body had decided that the Association should produce a monthly magazine at a low price for the benefit of the families of Britain who look to the medical profession not only for care in sickness but for guidance in health. This month the tenth anniversary issue of *Family Doctor* appears. It contains some admirable articles by leading authorities in several fields of medicine—articles which concentrate on prevention and reassurance just as much as on cure. Child health naturally receives particular attention, and Sir Arthur Porritt, P.R.C.S., immediate Past-President of the B.M.A., looks forward to the day when only accident surgery will remind us of the days of "cutting" surgery.

Family Doctor has not had a smooth passage during the ten years of its existence. Nearly all doctors now agree about the need for health education, but there are still many differences of opinion about the manner of carrying it out. The B.M.A.'s choice of "Health Education" as "the subject of the year" is a good one, and the views of Divisions and Groups are sure to be examined with interest by those engaged in this work. Meanwhile those responsible for the magazine will be encouraged by the messages of good will published in the tenth anniversary issue of *Family Doctor*—messages from, among others, Dr. Charles Hill, Chancellor of the Duchy of Lancaster; Dr. G. E. Godber, Chief Medical Officer of the Ministry of Health; and Sir Kenneth Cowan, Chief Medical Officer of the Department of Health for Scotland.

SURGERY IN RHEUMATOID ARTHRITIS

Under the auspices of the Empire Rheumatism Council a symposium on rheumatoid arthritis was held in the Hall of the Society of Apothecaries, London, on March 3. Twenty rheumatologists and twenty orthopaedic surgeons took part in it under the chairmanship of Dr. OSWALD SAVAGE (London) in the morning and of Mr. W. D. COLTART (London) and Mr. NORMAN CAPENER (Exeter) in the afternoon. This report deals mainly with the surgical aspects.

Indications for Surgery

Mr. W. D. COLTART (London), reviewing the indications for surgery, said that the surgeon's main responsibilities were the relief of pain, the correction of deformity, and the treatment of instability. Judgment was necessary to decide how each individual joint should be treated, but a bolder and earlier approach to multiple operations might well be rewarding. Mr. Coltart felt that further study of the predictability of joint involvement would be of great value, as it was of paramount importance that patients should not be worse off after operation. Most of them were conditioned towards conservatism in treatment, and loath to accept the need for operations such as arthrodesis. One of the major problems was the shortage of hospital beds and of rheumatology units in which patients could be cared for by experts. This point was strongly supported by Professor J. H. KELLGREN (Manchester), Mr. W. J. W. SHARRARD (Sheffield), and Dr. H. F. WEST (Sheffield). Professor KELLGREN also gave his views on the indications for surgery and said that it was wise to avoid operation during the acute phase of the disease, except where a tendon was ruptured or a knee-joint grossly disorganized.

Steroids and Surgery

The implications of systemic steroid therapy combined with orthopaedic surgery were discussed by Dr. P. S. DAVIS (London) and Dr. C. F. SCURR (London). Both agreed that the most important practical point was to continue drug therapy throughout the operative period and to give "booster" doses to cover the stress of the anaesthetic and the operation. Experience had shown that the usual therapeutic doses of corticosteroid drugs did not significantly modify tissue repair.

In the discussion it was agreed that all patients on corticosteroid therapy should wear a metal disk stating this fact.

Surgical Procedures

Mr. R. G. PULVERTAFT (Derby) dealt with the complex mechanical and physiological problems produced by rheumatoid deformities of the hand and wrist. He outlined the pathological changes which led to rupture of tendons, and the distension and erosion of joint structures resulting in subluxation and dislocation. Ulnar drift of the fingers was due to several factors, which included the instability of the metacarpo-phalangeal joints, the inability of the extensor hoods to move proximally, and the tendency of the extensor tendons to slide medially off the metacarpal heads. Mr. Pulvertaft believed that greater efforts should be made to operate on deformities at an early stage, and thought there was scope for procedures such as excision of affected synovial tissue, tendon replacement or transference, tendon release arthroplasty, and arthrodesis.

The place of appliances in the treatment of rheumatoid disease was then discussed by Mr. NORMAN CAPENER (Exeter). He said that they should be employed to relieve muscle spasm and pain, to give rest to acutely inflamed joints, and to prevent deformities or assist in their correction. There should be much more rest when the disease was active, but graduated with movement as it became quiescent. Plaster-of-Paris was the ideal material to use for this purpose, and there appeared to be little scope for complicated spring splints except in wrist deformities. This point was taken up by Mr. D. L. SAVILL (Edinburgh), who stressed the importance of "lively" splintage in correcting ulnar shift of the fingers. Mr. Savill also described the technique of carpal-tunnel decompression and synovectomy, and discussed the treatment of rheumatoid trigger finger and metacarpo-phalangeal deformities. In the latter condition he advised arthroplasty for women, but for men, where it was necessary to preserve strength, arthrodesis. Disabilities such as clawing and elevation of the toes in rheumatic disease required surgical correction, and Mr. Savill discussed the relative merits of excision of the proximal phalanges and amputation of all the toes. The latter procedure was favoured by Mr. D. R. SWEETNAM (London), who pointed out that the operation would be followed by some interference with the balancing mechanism, and warned that patients should be advised always to wear shoes of the proper length. Mr. K. I. NISSEN (London) differed in that he left the metatarsal heads, after removing their undersurface.

Arthroplasty of the Hip

At this stage the members of the symposium were instructed and entertained by Mr. JOHN CHARNLEY (Manchester), who spoke of his recent explorations into the problems of the surgical approach to the hip-joint. He said that after arthroplasty with the insertion of a Smith-Petersen cup the range of hip movement often diminished with time. In general this well-tried procedure was not suitable for the soft bone and poor muscles encountered in rheumatoid arthritis. A new technique he described involved replacement of the femoral head by a metallic prosthesis, which was arranged to work with extremely low friction against a socket of fluon ("teflon" or p.t.f.e), which lined the acetabulum. The steel prosthesis was bound to the bone of the shaft of the femur by means of cement, so that the body weight was diffused over a very large area of bone surface instead of creating a small number of extremely high pressure points, which was inevitable if the metal prosthesis was attached to the bone in the orthodox way. Mr. Charnley claimed that 75 patients who had undergone this operation since January, 1960, had received greater relief than was possible with the orthodox procedure.

Surgery of the Knee

The many problems associated with the surgery of the knee-joint were discussed by Mr. I. S. SMILLIE (Dundee). In selected cases he recommended synovectomy, which seemed to control the later development of osteoarthritis. In others, where lateral angulation with genu varum or valgus had taken place, linear osteotomy of the tibia was valuable, as it restored proper weight-bearing alignment. Arthroplasty of the knee-joint had received a fresh impetus from Walldius, who had devised a remarkable prosthetic joint. Another arthroplastic procedure using a simple steel mould applied to the lower end of the femur was described by Mr. GEOFFREY PLATT (Aylesbury), who said that he had obtained encouraging but not spectacular results with this technique.

HAEMOPHILIA SCHEME CENTRES

In 1954 a number of hospitals agreed, in collaboration with the Medical Research Council, the Ministry of Health, and the Department of Health for Scotland, to act as reference centres providing a registration service and diagnostic and treatment facilities which might be used, if desired, by general practitioners with haemophilic patients. The number of these haemophilia centres has gradually increased, and the following is an up-to-date list:

Aberdeen: Professor H. W. Fullerton, Department of Medicine, Foresterhill, Aberdeen. *Belfast:* Dr. M. M. Stevenson and Dr. M. G. Nelson, Department of Clinical

Pathology, Royal Victoria Hospital, Belfast. *Birmingham:* Dr. M. J. Meynell, United Birmingham Hospitals, General Hospital, Birmingham 4. *Bradford:* Dr. R. Turner, Royal Infirmary, Bradford. *Bristol:* Dr. A. B. Raper, Department of Medicine, Royal Infirmary, Bristol. *Cambridge:* Dr. F. G. J. Hayhoe, Haematology Clinic, Department of Medicine, Tennis Court Road, Cambridge. *Cardiff:* Professor H. Scarborough, Medical Unit, Royal Infirmary, Cardiff. *Carlisle:* Dr. J. S. Faulds, Cumberland Pathological Laboratory, Cumberland Infirmary, Carlisle. *Derby:* Dr. B. J. Leonard, Royal Infirmary, Derby. *Dundee:* Professor R. B. Hunter, Department of Pharmacology and Therapeutics, Medical School, Queen's College, Dundee. *Edinburgh:* Dr. R. H. Girdwood, Department of Medicine, University New Buildings, Edinburgh. *Exeter:* Dr. J. O. P. Edgcumbe, Department of Pathology, Royal Devon and Exeter Hospital, Exeter. *Glasgow:* Professor L. J. Davis, Department of Medicine, Royal Infirmary, Glasgow. *Hull:* Dr. A. J. Shillitoe, Royal Infirmary, Hull; Dr. L. S. Sacker, Department of Pathology, Kingston General Hospital, Hull. *Leeds:* Dr. W. Goldie, St. James's Hospital, Leeds 9. *Liverpool:* Dr. T. Black, Liverpool Royal Infirmary, Pembroke Place. Liverpool 3. *London:* The Hospital for Sick Children, Great Ormond Street, Dr. R. M. Hardisty; Postgraduate Medical School, Professor J. V. Dacie; The London Hospital, Dr. H. B. May; King's College, Dr. W. M. Davidson; St. Thomas's Hospital, Dr. G. I. C. Ingram; Lewisham Hospital, Dr. C. A. Holman; St. Bartholomew's Hospital, Dr. Bodley Scott. *Manchester:* Dr. J. F. Wilkinson, Department of Haematology, The Royal Infirmary, Manchester 13. *Newcastle upon Tyne:* Dr. H. Boon, Royal Victoria Infirmary, Newcastle upon Tyne 1. *Oxford:* Dr. R. G. Macfarlane, Radcliffe Infirmary, Oxford. *Portsmouth and I.O.W.:* Dr. J. R. O'Brien, Central Laboratory, Milton Road, Portsmouth. *Sheffield:* Dr. E. K. Blackburn, United Sheffield Hospitals, Department of Haematology, Royal Infirmary, Sheffield 6.

Nova et Vetera

PRIMITIVE PHYSIC

On November 1, 1724, John Wesley, then an undergraduate at Christ Church, wrote to his mother, "I suppose you have seen the famous Dr. Cheyne's 'Book of Health and Long Life' which is, as he says he expected, very much cried down by the physicians. He refers almost everything to temperance and exercise, and supports most things with physical reasons." Twenty-three years later when Wesley himself published *Primitive Physic,* a book which Dr. A. Wesley Hill says in his introduction "played its part in meeting a need that challenged Wesley in his reforming work in the eighteenth century," he drew heavily on Dr. Cheyne. Indeed, his thirty-one rules were by his own admission "chiefly transcribed from Dr. Cheyne."

In his twenty-page introduction to this useful reprint of Wesley's text,[1] the editor rightly sets it in the climate of its times. He includes a useful section on the various eighteenth-century theories of disease, illustrating their impact on Wesley from Wesley's *Journal.* He rightly calls attention to Wesley as a pioneer of hygiene and preventive medicine, as an optimistic advocate of electrotherapy, and as pointing a way to experiment and experience "out of obfuscating theories and pompous humbug."

It is perhaps a little captious to have hoped for a slightly ampler exploration of the basic bond that bound Wesley and Cheyne: a respect for William Law, the great eighteenth-century mystic. To Wesley, said one of his disciples, "Law came before the prophets," and certainly Cheyne's own remarkable conversion from being a riotous, porcine figure into the apostle of temperance was due largely to his reading of the mystics. But perhaps that would have carried the editor outside the scope of his purpose, which he has admirably fulfilled: to present us with an accurate scholarly text of the twenty-third edition of Wesley's great work. It played an integral part in kindling the social conscience of his day. It used to be said that Wesley saved England from revolution; it can also be said that he played his part in the lowering of the death rate which marked his century. One has only to look at Receipt No. 199, *The Scurvy.* Dr. Lind himself would have been pleased to see the reliance he placed on Seville oranges and garden cresses.

W. H. G. ARMYTAGE.

[1] *Primitive Physic.* By John Wesley. With an Introduction by A. Wesley Hill. (Pp. 127. 12s. 6d.) London: The Epworth Press. 1960.

New Appliances

A HYDRAULIC-POWERED, FOOT-OPERATED, TILTING OBSTETRIC BED

Dr. G. C. STEEL, anaesthetist, Queen Charlotte's Maternity Hospital, Royal Free Hospital, and Chelsea Hospital for Women, London, writes: Realization of the danger of inhalation of stomach contents during obstetrical anaesthesia, together with the demands of modern anaesthetic techniques, has emphasized the need for an obstetric bed specifically designed to tilt: firstly, in a head-down direction to deal with the unexpected regurgitation, and, alternatively, head upwards so that elective steps may be taken to prevent such disaster by passing an endotracheal tube in this position. In each case these movements must be initiated at the instant behest of the anaesthetist. With this in mind, I have designed a bed in which the interests of four people have been carefully considered: the patient, the midwife, the anaesthetist, and the obstetrician.

The bed consists of a horizontal rectangular tubular base a few inches off the ground, resting at each corner on a small wheel (Fig. 1). These wheels make the bed easily movable, but each can be rigidly locked by means of a simple foot-operated mechanism. From the lateral bars of this base spring two vertical support bars which hold up the bed surface proper at a pivotal point which is situated nearer to the foot end than to the head end. The head end is thus heavier, and, if unsupported, would tilt rapidly downwards, turning on the pivotal point.

The bed surface proper is divided into a head platform and a foot platform: the latter can be completely telescoped under the former when the patient is put in the lithotomy position. The mechanism has been specially strengthened so that the bed, when extended, is rigid enough to allow delivery in the left lateral position (Fig. 1). Here the convenience of the midwife has not been forgotten. The height of the bed, including the mattress, is 32 in. (81 cm.), the width is 30 in. (76 cm.). This allows the midwife to work well within her natural reach, which is much less tiring than working beyond it. Nor are these dimensions incompatible with the safety or comfort of the patient. The telescoping mechanism is of the simple push–pull variety: with constantly changing nursing staff, anything more complicated is quite unrealistic.

Determination of the relative lengths of the head and foot platforms presented a problem. Ideally, these should be such that the buttocks always lie on the division between head and foot platforms, so that lifting down the bed is not necessary when the patient is put in the lithotomy position. Two main factors militate against this: firstly,

the varying size of women; and, secondly, the fact that the foot end must be small enough to be wholly concealed under the head platform when closed up, so as not to hinder the obstetrician when applying forceps. Yet when this foot platform is extended, sufficient length of the runner forming

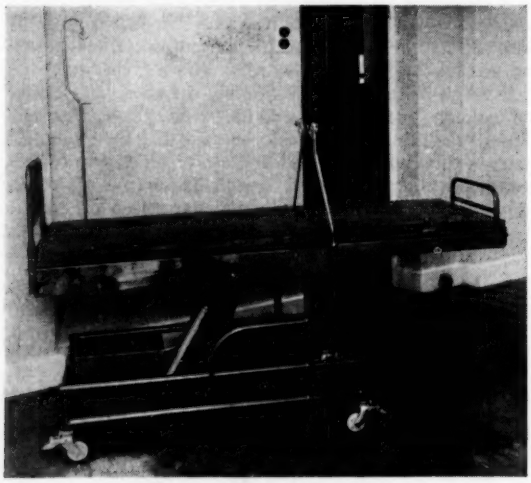


FIG. 1.—The bed extended.

the union between the two platforms must still be left under the head end to ensure that the extended foot platform is rigid and secure. A further consideration is that if the bed can be tilted head upwards in the extended position no vertical support for the foot platform is permissible.

To throw some light on this, 100 patients each had three measurements taken: (1) the normal head-to-foot in the prone position; (2) the run from head to foot when lying in the slightly curled up lateral position; and (3) the head-to-buttock measurement. These figures, wedded to engineering demands, resulted in a head platform 42 in. (107 cm.) in length, and a foot platform 27 in. (68.5 cm.) in length. Practice has shown that the overall length of 69 in. (175 cm.) is wholly adequate. The lifting of patients, while not wholly abolished, is minimal.

Each platform is covered by a foam mattress 2 in. (5 cm.) thick. This affords the patient complete comfort yet does not cause her to wallow in a valley. Small metal stops prevent the mattress from sliding when the table is tilted. In addition, it may be secured to the underlying platform by means of loops and buttons. When the foot mattress is removed it may be hung by its loops to hooks on the wall rather than be thrown on the floor. Since the normal tendency is for a mattress to slide off the bed when tilted, rather than for the patient to slide off the mattress, securing the latter as described appears to preclude the necessity for shoulder pads or a corrugated mattress.

For the application of forceps the obstetrician has an unimpeded approach to the patient. Each lithotomy pole is widely angled halfway up the shaft, and the hook holding the lithotomy stirrup at the top can be swung round and secured as desired on the inside or the outside. By turning each pole in its socket so that the angling brings the top inwards or outwards, and by adjustment of the stirrup at the top, the distance between the two stirrup hooks can be varied from 18 to 40 in. (45.5 to 101.5 cm.). Thus there is a wide range of adjustment for wide or narrow pelves.

Sockets are fitted around the bed for various purposes—for a small vertical foot end, for a small vertical head end, for the lithotomy poles, for the drip stand, and for shoulder pads if thought necessary.

The principle of the tilting mechanism is that the heavy head end of the bed surface proper is supported in the horizontal plane by a sealed column cylinder and piston unit which springs from a cradle slung between the bars of the base and runs up at an angle to support the underside of the head platform at a moving joint. If the piston is allowed to retract, the bed tilts rapidly in a head-down movement; if the piston is extended, the reverse tilt occurs. The range of this movement is approximately 25 degrees in elevation and 20 degrees in depression. A counterspring on either side of the piston unit prevents any possibility of its being pulled out as a result of weight being applied to the foot platform.

An efficient tilting mechanism for an obstetric bed should fulfil certain criteria. It should be controlled by the anaesthetist at the head of the bed and be foot-operated so as to leave his hands free to deal with the patient, and it must be equally efficient with the bed extended or closed. The head-down tilt must be very rapidly accomplished, yet gently arrested. The head-up movement, however, may proceed at a less urgent pace. The controls must be simple to operate and must be capable automatically of holding the bed steady at any angle of the tilt.

The two control pedals are at the head of the bed, conveniently placed for use by the anaesthetist's feet (Fig. 2). The one on the left has a pumping action and tilts the bed head upwards: cessation of pumping will hold the bed at that particular angle. The second pedal is on the right, and lifting it with the toe-cap opens the port in the hydraulic unit, causing a rapid head-down tilt. To prevent accidental initiation of this rapid tilt, the usual mechanism has been reversed. The foot pressed accidentally on the release mechanism has no effect, as it must be deliberately lifted from below. The linkage is countersprung so that the port is automatically closed as soon as the upward lift of the foot ceases, and movement stops instantly. The hydraulic mechanism, together with a spring stop, ensures that the tilt, however rapid, will be smoothly halted at any stage in

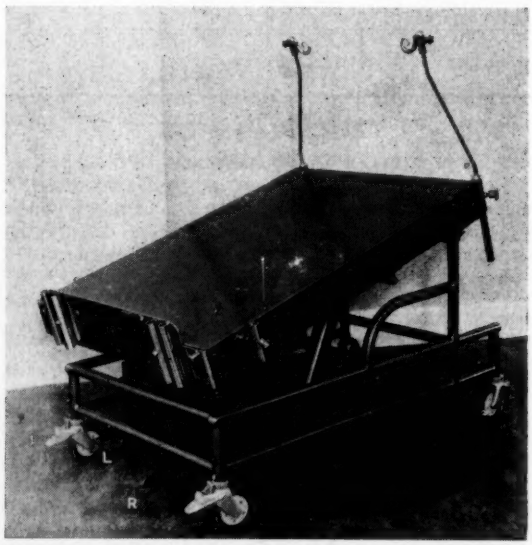


FIG. 2.—The bed in head-down tilt. L=Pump pedal. R=Release pedal.

its fall. The fall from the horizontal to the full tilt is achieved in 1.5 to 2 seconds. The lifting power of the piston is 1½ tons (1,524 kg.), and it is fully capable of holding the bed steady at any angle: but, for those who desire it, a safety support bar can be provided.

The prototype bed has been given deliberately hard use in the labour ward at Queen Charlotte's Hospital, and has acquitted itself well over a period of 10 months. My obstetrical colleagues and the labour-ward sisters have kindly

(Continued at foot of page 965)

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in common use.

Pyrvinium Embonate

"Vanquin" Suspension (Parke, Davis).

Composition.—This compound, for the treatment of threadworm infestation, is stated by the manufacturers to be 6-dimethylamino-2-[2-(2,5-dimethyl-1-phenyl-3-pyrryl) vinyl]-1-methylquinolinium embonate. It is a red crystalline cyanine dye, is very stable, and is only slightly soluble in water. It is put up as a strawberry-flavoured suspension which contains the equivalent of 10 mg. of the anhydrous base in each ml. of the suspension.

Pharmacology.—Given orally, vanquin is poorly absorbed from the intestine. It is well tolerated by rats and mice; a daily dosage of 198 mg./kg. body weight given to rats over a period of two to four weeks caused loss of appetite with a consequent fall in weight; a similar result was observed in mice given 50 to 125 mg./kg.; an increase of the dosage to 300 mg./kg. of body weight in these animals did not correspondingly increase these side-effects. The drug acted very effectively against the natural threadworm infections of both rats and mice. Its effect on the worms is thought to be due to inhibition of the enzyme systems which regulate their oxidative metabolism. Worms collected after subcurative dosage with vanquin showed evidence of respiratory depression and increased aerobic glycolysis. Depression of bone marrow and damage to liver and kidney have been observed in the experimental animal on large doses for long periods.[1]

Therapy.—Various workers have treated considerable series of patients with vanquin at dosages of 1.5 mg./kg. to 5 mg./kg. body weight daily for 1 to 10 days, or with a weekly dose for three weeks. The eradication rate of threadworm infestations after any of these dosages in all the series of patients treated with them has been reported to have been remarkably high (3 failures in 268 patients). Consequently it was concluded that a single-dose treatment of 5 mg./kg. of the base is sufficient. In practice this is said to have been the case. As a detected case of threadworm infestation is usually associated with undiagnosed infestations in the other members of the family and household, single doses for the patient's immediate household contacts are advocated. It is well to warn patients that immediately after the treatment the stools will be red, but that this is of no significance. Furthermore, in view of the notorious infectivity of this parasite, proper precautions must be taken to destroy eggs already contaminating personal and household linen in an endeavour to forestall reinfestation of those at risk.

Side-effects.—Nausea and vomiting may result from large doses. The drug should be given with caution to patients with renal or hepatic disease.

N.H.S. Basic Price.—16 fl. oz., 60s.

REFERENCE

1 American Medical Association, *New and Nonofficial Drugs*, 1960. Philadelphia.

(Continued from page 964)

expressed their satisfaction with it; patients, when questioned, have said that they are perfectly comfortable on it. To the anaesthetist faced with a hazardous emergency it is a welcome boon to have instant foot control of a tilting mechanism which operates either way.

The bed is manufactured to my expressed performance criteria by Messrs. S. B. Whitfield, 19 Conway Street, Fitzroy Square, London W.1. It is hoped that the cost will be in the region of £200.

In acknowledging my gratitude to the many people who have helped me with this idea, I would particularly thank Sister Fairbrother, of the labour ward, for her kindly tolerance and her invariably helpful suggestions.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Maternal Rubella

SIR,—Dr. Maurice Campbell commented in his interesting paper (March 11, p. 691) on differences reported by various workers in the rates of congenital defects following maternal rubella. This might be partly accounted for if rubella were not a specific infection but a syndrome with several possible causes. Exanthematous fevers resembling rubella but caused by various enteroviruses were discussed in your columns last year.[1] Many infections with E.C.H.O. type 9 virus, which was epidemic in Scotland in 1960,[2] resemble rubella closely. The occurrence of viraemia in this infection provides opportunity for the virus to reach the foetus. One investigation of E.C.H.O. 9 infection in Milwaukee in 1957[3] failed to show any marked increase of congenital defects following infection, but we have considered it worth while initiating a prospective study of the 1960 epidemic in Glasgow.

Dr. Campbell also discussed the possibility that foetal damage might arise when the mother was exposed to infection without overt attack. Experimental evidence of such an occurrence was accidentally obtained in this laboratory during studies of Coxsackie A7 virus. This virus was inoculated intracerebrally into an adult female merion, not known to be pregnant. The merion remained in normal good health, but 12 days after inoculation a dead newborn merion was found in the cage. By subinoculation into suckling mice, this dead foetus was found to be heavily infected with Coxsackie A7 virus.

—We are, etc.,

N. R. GRIST.
JOAN B. LANDSMAN.
CONSTANCE A. C. ROSS.

Departments of Virology and Infectious Diseases, Glasgow University.

REFERENCES

1 *Brit. med. J.*, 1960, **1**, 1794.
2 Landsman, J. B., MacAnespie, H., Weetch, W. J., and Bell, E. J., *ibid.*, 1960, **1**, 464.
3 Peterson, J. C., and Glicklich, L., *Amer. J. Dis. Child.*, 1960, **100**, 779.

Prognosis after Hemiplegia

SIR,—The paper by Dr. G. F. Adams and Mr. J. D. Merrett (February 4, p. 309) throws interesting light on many facets of this difficult problem. I should, however, like to reinforce the views of Dr. J. B. Millard (February 25, p. 588). The results of treating 115 hemiplegic patients at this medical rehabilitation centre during the past three years show that positive benefit accrues to a large proportion of the patients. They represent approximately 9% of the total number of patients discharged during this period. This may have some bearing on the results achieved, as it is important to rehabilitate such patients in an active therapeutic community where the balance of long-term to short-term patients is approximately 40% to 60%.

The patients were "selected" in the sense that they were referred to this centre for treatment. Only patients with severe hypertension were considered unsuitable. Many patients had lived a life of total dependence for a considerable period before being referred for treatment. Unfortunately many such patients are only referred to this centre as part of a "salvage operation" rather than

as a planned step in their intensive rehabilitation. The results may be summarized as follows:

Discharged to original work	18
Discharged to different work	24
Referred to disablement resettlement officer for placing	7
Discharged to training centre	3
Discharged home—fully independent	34
Discharged home—partially independent	11
Referred to hospital for further treatment	17
Self-discharge	1
	115

An optimum result was obtained in 74.7% of the patients discharged during this three-year period. During 1958 and 1959 a follow-up, after a three-month period, of the 29 patients who were discharged to work showed that 22 were still working, five were again unemployed, and two did not reply.

All these cases were treated as out-patients on a whole-day basis, five days a week. There is now little doubt that it is only by such intensive overall treatment of the patient, together with a close liaison between all the statutory and voluntary agencies concerned, that really significant results can be achieved.—I am, etc.,

Medical Rehabilitation Centre, London N.W.1. JAMES G. SOMMERVILLE.

Longevity of Haemophiliacs

SIR,—I was very interested to see the encouraging data on the longevity of haemophiliacs in Dr. F. Nour-Eldin's letter (March 18, p. 824). This situation can only improve as further therapeutic accuracy is developed and as more and more mild cases are diagnosed.

One problem that faces a sufferer is the fact that nobody labelled as a haemophiliac is considered a possible life-insurance risk. This state of affairs is understandable, but bears further investigation. Certainly some of the milder haemophiliacs may suffer no disability until abnormal bleeding occurs post-operatively or after severe trauma.[1] For this reason many such cases, or even whole families, may remain permanently unsuspected and undiagnosed.

Is it not time that the word "haemophiliac" was defined more precisely? There is at present no clear distinction between the very mild sufferer and the normal person with a low level of antihaemophilic globulin. An arbitrary classification could be devised according to the level of antihaemophilic globulin—for example, (*a*) 0–2%—severe haemophilia; (*b*) 3–15%—mild haemophilia; (*c*) 15–30%—occult haemophilia; and (*d*) 30% and over—range of normality. Clinically, these can be divided as follows:

	Incapacity in Ordinary Life	Joint Deformity	Excessive Bleeding	
			Everyday Life	Surgery or Trauma
(a)	Severe	+	+++	++++
(b)	Slight	—	+	+++
(c)	—	—	—	++
(d)	—	—	—	Perhaps slight in lower ranges

These four groups of people all present different clinical problems and should be considered individually in assessing prognosis. All but the first group, provided reasonable precautions are taken, should stand a good chance of reaching their allotted threescore years and ten.—I am, etc.,

Central Middlesex Hospital, London N.W.10. A. F. H. BRITTEN.

REFERENCE

1 Aggeler, P. M., Hoag, M. S., Wallerstein, R. O., and Whissell, D., *Amer. J. Med.*, 1961, **30**, 84.

Megaloblastic Erythropoiesis in Haemolytic Anaemia

SIR,—I read the paper by Drs. I. W. Delamore, J. Richmond, and S. H. Davies (February 25, p. 543) and was particularly interested in their second case in view of the opinion expressed that this case is unique in so far as megaloblastic erythropoiesis was present in congenital spherocytosis in the absence of pregnancy. I described a case[1] in a boy aged 8 years with congenital spherocytosis with an atypical marrow in which the majority of the nucleated red cells appeared as megaloblasts. It is of some importance that in both of these patients the megaloblastic change was found during the recovery period following an aplastic phase. The aplastic crisis was originally described by Owren[2]; I suggested that marrow exhaustion may follow the prolonged active erythropoietic stimulation present in haemolytic anaemia although the mechanism is not fully understood. The phase of recovery is usually associated with hyperactive erythropoiesis and there may be a temporary relative insufficiency of "haemopoietic factor." Chanarin *et al.*[3] have shown that there is probably a deficiency of folic acid.

It is becoming accepted that megaloblastic erythropoiesis may occur in many varieties of haemolytic anaemia, and references are given in the paper by Dr. Delamore and his colleagues. Further examples in sickle-cell anaemia are given in Dr. S. Shaldon's medical memorandum (March 4, p. 640). Other references in haemolytic anaemia are Turnbull,[4] Ohlsen and Roelsen,[5] and Miesch, Baxter, and Levin.[6] It should be added that Turnbull's evidence is based on marrow examinations after necropsy, which is admittedly somewhat unsatisfactory. On the other hand, Dacie and White[7] refer to macronormoblastic and not megaloblastic erythropoiesis in haemolytic anaemia.—I am, etc.,

Charing Cross Hospital and Medical School, London W.C.2. SIDNEY SHAW.

REFERENCES

1 Shaw, S., *Proceedings of the 7th International Congress of Haematology*, 1960, Vol. 2, part 1, p. 437. Il Pensiero Scientifico, Rome.
2 Owren, P. A., *Blood*, 1948, **3**, 231.
3 Chanarin, I., MacGibbon, B. M., O'Sullivan, W. J., and Mollin, D. L., *Lancet*, 1959, **2**, 634.
4 Turnbull, H. M., in Vaughan, J. M., *The Anaemias*, 2nd ed., 1936, p. 243.
5 Ohlsen, A. S., and Roelsen, E., *Acta med. scand.*, 1943, **114**, 383.
6 Miesch, D. C., Baxter, M. R., and Levin, W. C., *A.M.A. Arch. intern. Med.*, 1957, **99**, 461.
7 Dacie, J. V., and White, J. C., *J. clin. Path.*, 1949, **2**, 1.

Service Overseas

SIR,—I have read the correspondence concerning overseas service with great interest. After qualifying I worked in Uganda, where I had much more responsibility than I would have had at a similar stage in England, and saw many interesting cases that one no longer sees in England. On returning to England I found it difficult to get a post that I wanted, as preference was given to those who had been working in the larger teaching hospitals in England.

I read that it was being advocated that overseas students should have a chance to work in British hospitals, and I feel that it would be most valuable for those returning from a tour overseas to be able to work for a time in a teaching hospital or some other hospital where standards are high. Overseas facilities are

frequently limited, patients numerous, and medical staff few. Diagnosis is on the greatest probability and often not open to proof. One is often isolated and has little chance to exchange experiences or discuss problem cases with other doctors. This tends to create an attitude of either *laissez faire* or infallibility which is difficult to counteract alone. Would there be a possibility of some scheme whereby overseas doctors returning on leave had some kind of practical "refresher course" so that they could be stimulated to maintain high standards and work for better facilities when returning overseas?

A further point is the question of employment of women doctors. I have accompanied my husband to Bechuanaland, which is a territory short of doctors and medical facilities. Before leaving England I inquired of the possibility of work with the government. The vacancies were only for men. The local hospital is often short of one of the two doctors as there are dispensaries to visit, and at present plague near S.W. Africa also requires a doctor. There are four women doctors who are in the territory as wives. Some of the government work involves a great deal of travelling over bad roads, but surely there is a place for women doctors which could be mainly in a hospital? Also it would be more economical as they could be regarded as locally recruited.—I am, etc.,

Serowe, Bechuanaland. THERESA E. PIPER.

Erythromycin

SIR,—Your leading article, "Indications for Erythromycin" (February 25, p. 563), stated that hypersensitivity is never a bar to its use. A recent case suggests otherwise.

The patient was a woman of 68 with a chronic paronychia. Crystalline penicillin by intramuscular injections of 500,000 units twice daily was producing rapid improvement, but on the fifth day a generalized maculo-papular rash appeared. Cessation of penicillin and treatment with antihistamines led to disappearance of the rash in three days. One week later the paronychia flared up again and treatment was initiated with tab. erythromycin., mg. 250, four times a day. In 24 hours a similar generalized eruption appeared and responded promptly to antihistamines and withdrawal of erythromycin.

Allergic reactions to erythromycin are rare and it is even more rare to find a common sensitivity to both penicillin and erythromycin. The possibility of a cross-sensitization between penicillin and erythromycin is worthy of consideration, especially as erythromycin is likely to be used more freely.—I am, etc.,

London E.10. J. SAPERIA.

Oral "Persantin"

SIR,—No doubt many of your readers will have received during the past few weeks some lavish advertisements of a new drug called "persantin" which is claimed, largely on the basis of work in experimental animals, to be effective as a coronary arterial dilator. This advertising material recommends the use of the drug both parenterally and orally in a variety of cardiovascular conditions. I cannot comment on most of these recommendations as I have no personal knowledge concerning them.

One of the suggested uses of the drug is orally, in a dose of 25–50 mg. three times a day, in patients with angina pectoris. I feel it is my duty to report that some months ago we conducted, at the request of the manufacturers, a double-blind trial of this preparation in 25-mg. doses in six patients with angina pectoris: the patients acted as their own controls, receiving alternately the drug and placebo, and the trial continued over periods averaging about twelve weeks. The results were assessed in terms of the number of attacks of pain recorded each day, and were negative in the sense that there was no observable difference between the placebo and the drug: the trial was discontinued. The results were acknowledged by the manufacturers to show no effect from the drug. In later correspondence they invited us to carry out trials using parenteral administration, and commented, "It is in fact now becoming clear that with the dosages we have hitherto employed it is very difficult indeed to demonstrate any objective effect from persantin given orally."

I would like to suggest that further evidence of the clinical effectiveness of this drug is required before its oral use should be advised in the management of myocardial ischaemia.—I am, etc.,

Cardiac Department, Guy's Hospital, London S.E.1. D. C. DEUCHAR.

Hazard of Endotracheal Intubation

SIR,—We wish to report a bizarre complication of endotracheal intubation.

The patient was a 30-year-old woman weighing 53 kg. and born in Morocco. She was suffering from an acute inflammatory process of the left parotid gland of several days duration. Physical examination revealed a large very tender swelling of the left parotid area. A thick, pus-like fluid was expressed from Stenson's duct on external pressure. The temperature was 37.2° C. Chronic bilateral otitis media was the only other positive finding.

Her condition did not yield to conservative treatment, including antibiotics, and it was decided to carry out a surgical exploration of the area. She was prepared with morphine, 10 mg., and scopolamine, 0.25 mg., by subcutaneous injection, one hour before operation.

Induction was with sodium thiopentone, 0.4 g., followed by succinylcholine, 75 mg. After inflation of the lungs with oxygen, intubation with a No. 10 Portex tube was performed, facilitated by the use of a malleable stylet. Anaesthesia was continued using nitrous oxide/oxygen/trichlorethylene delivered from a Boyle's apparatus. A vertical incision was made in the pre-auricular region. The

No. 5 Portex endotracheal tube inside a No. 10 tube.

parotid capsule was very tense, but on opening no pus was found. At the end of operation endotracheal suction with a gum-elastic catheter was carried out prior to extubation. The duration of anaesthesia was 35 minutes, and before the patient left the theatre she had sufficiently recovered to open her eyes in response to hearing her name. Her colour was normal and respiration appeared satisfactory.

On the morning after operation the patient was found to be suffering from sore throat, difficulty in swallowing, and aphonia. Examination of the throat revealed redness and excessive secretions in the oro-pharynx. The condition was attributed to the infective process, possibly exacerbated

by the trauma of intubation. The symptoms became progressively worse over the next 24 hours. Indirect laryngoscopy at this stage revealed a circular greyish-white foreign body protruding between the vocal cords. This was removed with forceps and found to be a No. 5 Portex endotracheal tube. The patient was relieved immediately and from then on made an uninterrupted recovery. Three days later further indirect laryngoscopy revealed slight inflammation of the larynx with normal movements of the cords.

The finding of a No. 5 endotracheal tube in the larynx 36 hours after intubation with a No. 10 tube could be reasonably explained in only one way: the smaller tube must be presumed to have been introduced within the larger, in which it fits quite snugly (see Fig.). Trials showed that displacement of the inner tube could be easily effected by a simple gum-elastic suction catheter, and this is believed to have occurred in our case. Unexpected objects in the lumen of endotracheal apparatus are not always easy to detect before use and have been the cause of acute respiratory obstruction.[1 2 3]

In the case here described, although the lumen of the endotracheal tube was markedly reduced by the tube within, no signs of respiratory difficulty were noted during anaesthesia, and a very surprising feature was the fact that this large foreign body remained in the respiratory tract for 36 hours without causing violent respiratory upset. The clinical features of the case would suggest that the upper end of the tube remained, for the whole 36 hours, in the larynx. The length of the tube is 15 cm., so that its lower end could be presumed to have been held up at or near the bifurcation of the trachea.

It is apparent from this case and from that described by Jenkins[3] that the free passage of a stylet through an endotracheal tube is no guarantee of the complete patency of that tube. The best form of check is by inspection, and this would be greatly facilitated by the use of transparent material in the manufacture of endotracheal tubes and connectors.—We are, etc.,

Hadassah University Hospital, Jerusalem, Israel. J. T. DAVIDSON. M. FEINMESSER.

REFERENCES

1 Hewer, C. L., *Brit. med. J.*, 1956, **2**, 766.
2 Haselhuhn, D. H., *Anesthesiology*, 1958, **19**, 561.
3 Jenkins, A. V., *Lancet*, 1959, **1**, 761.

Liver Abscess After Perforation by Fish Bone

SIR,—The report by Dr. N. D. Gower and his colleagues (February 18, p. 475) of a man with a liver abscess following perforation of the liver by a fish bone reminds me of a similar case seen nearly 20 years ago in Dewsbury. In view of the extreme rarity of such cases a further short report seems worth recording.

The man, about 50 years old, was admitted to Staincliffe General Hospital with deep jaundice and high fever. The only history available was that he had been a fit man up to four days before admission, when he had begun to complain of vague malaise, developed jaundice, and deteriorated rapidly. Examination confirmed the jaundice and showed dehydration and tenderness in the epigastrium. He died within 18 hours without a diagnosis having been made. At the post-mortem examination, ordered by the coroner, the end (15 mm. long) of a slender bone (50 mm. by 5 mm. by 3 mm.) was seen protruding into lumen of the stomach at a point two-thirds of the way down the lesser curvature. Dissecting along the bone showed the distal end to be lying in the abscess cavity (60 mm. diameter) in the lesser omentum. Multiple abscesses of varying sizes were present in the liver.

It was only later that the bone was identified as being part of the skeleton of a rabbit. The patient's wife then volunteered the information that four days before her husband's death rabbit had been the main course for their Sunday dinner. She denied that the patient had had any difficulty during the meal or that he had complained of any pain subsequently.

This case bears close similarity to that of Dr. Gower and his colleagues, but in my case the site of perforation of the stomach was obvious.—I am, etc.,

Leeds 1. LEONARD ROSENTHAL.

"Marbadal C" and Gonorrhoea

SIR,—There is evidence that the incidence of gonorrhoea has risen in Britain. In view of this, the indiscriminate use of "marbadal C" vaginal tablets may be associated with an element of risk. These tablets include in their composition 0.5 g. of sulphatolamide, and this latter drug may be responsible for the masking of early cases of gonorrhoea.

A clinical investigation was arranged in this department to prove or disprove this point. A young woman in whom gonorrhoea had been excluded by films and cultures was given a course of marbadal C tablets as recommended by the makers. No tampons were used. This patient was not receiving any systemic sulphonamide therapy. On the sixth day of treatment the following procedures were carried out. High vaginal secretions were collected on standard filter-paper disks; the vagina was then swabbed clean and the fornices packed with swabs; further tests were taken from the cervical canal about 1½ in. (3.7 cm.) up from the cervical os. The bacteriological report was as follows: Vaginal and cervical secretions absorbed into standard filter-paper disks gave large zones of growth inhibition on cultural plates seeded with *Neisseria gonorrhoeae* and *Bact. coli*. Antimicrobial action approximately equivalent to: *vaginal secretions*—10 mg. sulphonamide/ml.; *cervical secretions*—5 mg. sulphonamide/ml. The vaginal concentrations might possibly have been higher if tampons had been used.

These concentrations would invalidate the results of high vaginal smears for gonococci, as taken by some doctors, and also interfere with the recommended intracervical smears in diagnosing a gonococcal infection. I would suggest that these tablets should not be used locally where the possibility of gonorrhoea exists or during the observation period of known gonococcal contacts. It might help if the manufacturers of marbadal C mentioned specifically gonorrhoea in their pamphlet, as doctors should diagnose the condition in its early stages and not delay until pelvic complications arise.

I am most grateful to Dr. T. B. M. Durie, of the Royal Infirmary Bacteriology Department, for his help and co-operation.

—I am, etc.,

Department of Venereal Disease, Edinburgh Royal Infirmary. M. SCOTT GRAY.

Lavatory Seats

SIR,—Surely, with venereal disease on the increase, someone should draw attention to the fact that in most of the lavatories of British Railways and of London Passenger Transport waiting-rooms and in the women's public lavatories of the London streets (and doubtless of many of our other cities) the antiquated type of seats

are still being used. It is time that a protest was made, and that, particularly for the protection of small girls who inevitable wriggle up on to a lavatory seat, the old-fashioned wooden oval should be replaced by the horseshoe-type of seat so much less liable to spread infection.—I am, etc.,

London S.E.17. YOLANDE FRIEDL.

Release of Bacteria from Surgeons' Hands

SIR,—This problem of the disinfection of the hands has interested me for some time.[1-3] The method I advocate is somewhat similar to the one described by Mr. L. W. Stuttard (February 25, p. 591). I advise the person to wash his or her hands under a running hot-water tap with toilet soap, dry the parts carefully with a sterile towel, and then soak the fingers and hands in 0.5% chlorhexidine digluconate in 95% industrial methylated spirit or in 0.5% hexachlorophane in 95% industrial methylated spirit for at least 60 seconds. The hands are then waved about in the air to dry, which takes about two minutes, and then powdered with sterile rice-starch powder and the sterile gloves put on.

In addition to care in the sterilization of the hands, I am an advocate of gloves for nurses.[4] Much of the infection that is carried from patient to patient with mysterious regularity could be prevented if more care was taken in the sterilization of hands, and sterile gloves were compulsory wear for nurses as well as surgeons, and probably food-handlers, too.—I am, etc.,

St. Margaret's Hospital, Epping, Essex. FRANK MARSH.

REFERENCES

1 Marsh, F., *Brit. med. J.*, 1960, **1**, 1809.
2 —— *Lancet*, 1960, **2**, 709.
3 —— ibid., 1958, **2**, 1236.
4 —— ibid., 1958, **2**, 588.

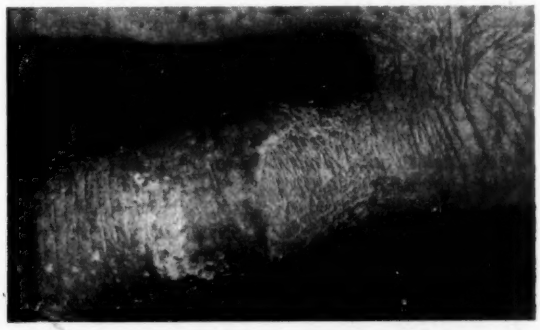
Tubular Bandages

SIR,—"Tubegauz," the seamless tubular gauze bandage, is now widely used. It has many advantages over the more conventional open-wove bandage and is a useful method of covering a dressing.

Having watched the use of this type of bandaging for some time, I feel that it has two great dangers which have serious consequences. Firstly, when the tubegauz is being applied the proximal edge is turned by a twist which causes the gauze to grip. If the nurse turns, twists, and pulls at the same time, she produces tightening. If one edge is superimposed on another, then a serious constriction may occur. If this does not produce severe pain due to ischaemia, it will often delay healing by reducing the blood supply. When used on fingers it may produce oedema and resultant stiffness when the retained fluid becomes organized. This trouble can be overcome by correct bandaging technique and the use of the correct number of layers. This danger is emphasized by the manufacturers. Nevertheless, it is a point which requires constant vigilance on the part of those who instruct nurses in the use of tubular bandages.

The second point occurs when the tubegauz is used without adequate padding as a primary dressing. After the initial surgery or dressing of a wound or other lesion, especially on the fingers, the fact that swelling will and must take place should not be forgotten. If the tubegauz is pulled and turned at the same time, a pressure dressing will result. This is most dangerous and undesirable. If the layer of wool under the tubular bandage is very meagre, it will not be able to protect the underlying tissues from the pressure as the swelling takes place.

Both these faults are easily corrected, but the results of poor technique are so serious that these dangers must be constantly and emphatically pointed out to all who use this method of bandaging. Those who supervise industrial and other dressing-stations must be ever watchful. Misuse of tubegauz brings delayed healing and chronic oedema as the photograph demonstrates.



It shows a finger that has been dressed with tubular bandage. The constriction is easily seen. The finger was also stiff. This need not have occurred and its correction will take time.—I am, etc.,

Bristol 8. H. K. BOURNS.

Clinic Doctors

SIR,—Having set an hour a week aside for the last five years to run my own antenatal and child welfare clinic, I must agree with Dr. Edward L. Moll's letter (March 4, p. 671). The satisfaction I have found from it has been great. I am also permitted to distribute welfare foods to my own patients but have not as yet negotiated for a public health nurse to be present as recommended in Taylor's *Good General Practice*.[1] The time from 2.30 to 3.30 p.m. coincides with a relatively free period in the family woman's day and the absence of the normal waiting-room patients adds encouragement to use this special session.

Without adding to the large number of complaints of overlapping of services, and in an effort to be constructive, may I suggest that all school medical examinations be discontinued, except the initial one at about 5 and a final one in the school-leaving year? Alternatively, an option should be given to parents to refuse all school medical examinations except the ones I have mentioned. I am more than ever convinced that the public health authorities' main job is to ensure a high immunity state of the population at the expense of running duplicating clinics of various kinds. It is a sobering thought that 12½ years after the introduction of the Health Service personal immunization cards are only available from the much-maligned drug firms. No central or local authority has yet grasped the opportunity of making this simple introduction. I reckon the cost to be £300,000 plus postage for everybody to receive one—or they could be collected at Post Offices.—I am, etc.,

Llandrindod Wells, Radnorshire. H. J. HOUGHTON.

REFERENCE

1 Taylor, S., *Good General Practice*, 1954. Oxford Univ. Press, London.

SIR,—Your correspondent, Dr. W. H. Crichton (March 11, p. 746), is, I am sure, quite right, that the average mother when taking her child for immunization, prefers a "congenial and homely atmosphere in the company of healthy babies and their mothers to a dreary surgery in the company of chronic bronchitics." The implication, however, that infant welfare clinics are always congenial and homely and doctors' surgeries always dreary and full of sick people cannot go unchallenged. I have been to several infant welfare clinics in large draughty church halls, and, however friendly the staff, the atmosphere can hardly be called homely. By contrast many doctors' waiting-rooms are bright and friendly.

In my experience most general practitioners who carry out many immunization procedures do so at certain specified hours outside the usual surgery times. Many of us have afternoon baby-clinics to which mothers are encouraged to bring their healthy babies, and arrangements are made for older children to attend for booster injections, etc., on their way home from school. In this way no lessons are missed and they are seen before the evening surgery. It is often worth the extra time and trouble, where there is a large family and a harassed mother, to carry out immunization procedures in the home, and a general practitioner can more readily do this than a clinic doctor. Now that appointment systems are being used more and more in general practice Dr. Crichton's picture of a mother waiting to have her child immunized in a dreary waiting-room full of chronic bronchitics must be the exception. There may still be a place, though a limited one, for infant welfare clinics, but in a well-run general practice I submit that the best person to carry out immunization procedures is the family doctor.—I am, etc.,

South Croydon, Surrey. ELEANOR M. SAWDON.

*** This correspondence is now closed.—ED., *B.M.J.*

Aetiology of Ulcerative Colitis

SIR,—I was most interested in the symposium on ulcerative colitis (January 21) and I appreciate that these papers describe the practical problem of physicians and surgeons in this extremely difficult condition. I was also most interested in Dr. Hugh Gainsborough's subsequent letter (February 11, p. 425). I entirely agree with him that the psychiatric aspect should be taken much more into consideration. I think he is probably perfectly right when he says that patients suffering from this disease have got a fairly well marked personality pattern.

As a psychiatrist I think one of our major problems is a lack of specialized knowledge about this particular condition. Looking back on my own experience I can only remember three or four cases which I dealt with for ulcerative colitis itself. Of the three or four cases which I have seen I can remember two which were helped by psychiatric treatment. I certainly wouldn't claim anything from such small numbers as this, but I would also like to question the number of cases which Dr. G. Watkinson (January 21, p. 147) had studied which had been made worse by the use of psychotherapy in the acute stage. I think that the time has come when the so-called psychosomatic group of diseases should be carefully studied by physician, surgeon, and psychiatrist so that a concerted attack may be made on such serious conditions as ulcerative colitis.—I am, etc.,

London W.1. W. B. KNAPMAN.

Oral Treatment of Diabetes

SIR,—I cannot agree with Dr. E. F. B. Cadman (March 4, p. 672) that, provided the second pre-breakfast specimen of urine is sugar-free, the amount of glycosuria of diabetics during the rest of the day is immaterial. This specimen may be negative in a mild untreated diabetic. I presume Dr. Cadman would not say that no treatment is necessary in such a case.

Though in many cases insulin injections are life-saving, or essential for the maintenance of reasonable health, they are a crude substitute for the adequate physiological secretion of insulin from the islets of Langerhans. With insulin injections, therefore, it is hardly to be expected that the blood sugar can be maintained throughout the 24 hours, between the upper and lower limits of physiological normal. Some glycosuria, reflecting a raised blood sugar, has to be tolerated, therefore, as the lesser of two evils, of which the other, needless to say, is hypoglycaemia, with its unpleasant and incapacitating symptoms.

Where there is a successful response to the drug, treatment with an islet-stimulating sulphonylurea would be expected to restore an adequate secretion of endogenous insulin, manifested by the absence of significant glycosuria throughout the 24 hours. This is, in fact, the criterion of a satisfactory response to these drugs.[1]

On administration of a sulphonylurea, the tablet-test for glycosuria daily three times a day is advisable. Once glycosuria is controlled, the three tests need be performed on only one day per week or per month, or on return of any diabetic symptom. Patients do not find this a burdensome multiplication of tests. An insignificant amount of glycosuria giving a positive reaction with a test paper could be misinterpreted if this test is used. I cannot see the use of these papers, therefore, in the routine control of diabetes.—I am, etc.,

Barton-on-Humber, Lincs. S. H. F. HOWARD.

REFERENCE

[1] Bloom, A., 1960, personal communication.

Occupational Burn

SIR,—I was most interested in Mr. A. Dickson Wright's letter (December 24, 1960, p. 1885) about the cigarette burn on the abdominal wall. It reminds me of an occasion in the early thirties when I was surgeon on a luxury liner making a world cruise. The smoke-room steward attended the surgery on the morning after calling at an Asian port, where he had spent the day ashore with the passengers. I should explain that this official is perhaps the most important (and certainly the richest) member of the crew in the passengers' eyes. On my asking him what the trouble was he replied, "Doctor, I've got two navels!" This was indeed true, for he had gone to sleep, or rather into coma, under the influence of a large intake of alcohol of some exotic brand, with a cigarette burning in his hand. The burn was just above the umbilicus, and similar in every respect to that described by Mr. Dickson Wright, but was very slow in healing. It was many years later that I discovered, as an industrial medical officer in the non-ferrous metal industry, that excision and suture was the treatment of choice in small deep burns with total skin destruction such as those caused by molten metal splashes.—I am, etc.,

West Moors, Dorset. NEIL G. MARR.

Cigarette in the Mouth

SIR,—Since I entered practice in this district six years ago there have been five cases of carcinoma of the lung, all occurring in men. Out of these five men, three have been barbers. While taking into account that carcinoma of the lung is a common condition and hairdressing a not unusual occupation, the incidence seems unduly high. On mentioning it to my partner, it was his impression, too, that he had seen the disease and the occupation occur together. I am interested to discover whether any other practitioners have noted this association, and whether anyone has any suggestions as to the possible relationship.

It has been noted that the absence of inhalation of cigarette smoke is no protection against the development of lung cancer; indeed, I believe some figures suggest that inhalation seems to impart some protection. I have noticed that many people who boast of not inhaling commonly allow the cigarette to burn away in the lips so that, in fact, the period during which their bronchial mucosa is exposed to smoke is probably greater than in those who inhale and immediately exhale the smoke. Perhaps the fact that barbers who smoke while they are working tend to smoke in this manner, since they have both hands engaged, may be the answer. Certainly of the three men whom I have known two smoked in this fashion. The wife of one of them said to me, "He used to go out with a cigarette in his mouth in the morning and came in with a cigarette in his mouth in the evening"—not "smoking" but "with a cigarette in his mouth."—I am, etc.,

Kingston-on-Thames, Surrey. GWILYM EVANS.

Marking the Skin

SIR,—I am surprised at the number of surgeons who have never been blackberrying themselves, or observed the results on others. The inevitable superficial scratches present as thin red lines the following day. No amount of washing, scrubbing, or application of unguents, solvents, or antiseptic lotions will remove the marks.

If the sites for incision over varicosities (March 18, p. 830) are marked the day before operation with a sharp needle, firmly enough to scratch the epidermis, but without drawing blood, no paints or dyes or magic formulae are needed. If there is a danger of the marks being confused with the results of traumatic preparatory shaving, then a few short cross-scratches in addition serve to make the distinction clear. The procedure is painless and foolproof, and I have used it for years. I make no claim to originality: indeed I would be glad to learn what simple genius thought of it first.—I am, etc.,

Plymouth, Devon MICHAEL REILLY.

POINTS FROM LETTERS

Guide to Portsmouth

Mr. VICTOR W. P. GALPIN (10 Bembridge Crescent, Southsea, Hants) writes: I am very keen on obtaining a copy of the Guide and Handbook of Portsmouth that was issued to those medical gentlemen who attended when the B.M.A. held their Conference here in 1899. There are three or four copies in the reference department of the Central Library, but I am most anxious to have a copy for myself. I have lived here for nearly 74 years and am very interested in the history of this city.

Obituary

I. H. McCAW, M.D.

Dr. I. H. McCaw, physician in charge of the dermatological department, Royal Victoria Infirmary, Belfast, and a former president of the British Association of Dermatology, died on March 17 in Belfast. He was 64 years of age.

Ivan Henry McCaw was the only son of the late Dr. John McCaw, a pioneer paediatrician in Belfast, whose book on diseases of children is still in use. Educated at the Belfast Academical Institution, he was a medical student at the beginning of the first world war and was commissioned in the Royal Irish Rifles and was badly wounded during the Battle of the Somme. Returning to Queen's University, Belfast, he graduated M.B., B.Ch., with honours, in 1922, proceeding M.D., with commendation, in 1933. After graduation he held several resident posts at the Royal Victoria Hospital and then went to Edinburgh and to Guy's Hospital, London, for postgraduate study of dermatology. On his return to Belfast he was appointed dermatologist to the Royal Victoria Hospital, the Royal Belfast Hospital for Sick Children, and other hospitals in Northern Ireland. He was president of the British Association of Dermatology in 1948, and a member of the Dermatological Group Committee of the B.M.A. from 1947 until the time of his death.

Mr. IAN FRASER writes: The staff of the Royal Victoria Hospital, and, in fact, all Ulster, mourn the death of Dr. Ivan McCaw at the age of 64. It was in 1917 at Messines, when as a young second lieutenant of 19 years of age, carrying the flag of his unit, he was wounded by a sniper's bullet. He returned home, but with his right arm partially paralysed by a brachial-plexus injury, and as a consequence he had to forgo his ambition to be a surgeon for the less strenuous one of a dermatologist. How well he succeeded in this branch is well known throughout Great Britain. He built up a department second to none, and he has trained a band of keen and active successors.

Ivan McCaw's success came from his gentleness, his humility, and his love for mankind—for his patients, his friends, and his colleagues. His courage in persevering with golf and other games made him admired by all, and some years ago he was elected captain of the Royal Co. Down Golf Club. His friendship was greatly valued by us all, and his wise counsel always carried the day.

The funeral service in the local cathedral where he worshipped was attended by his many friends from all over Ulster. It gave them an opportunity to show in public what they had felt for years in private. Although his professional life was a full one, his main interest was his home. He was never happier than when he was with his wife, his daughter, and his son. To his wife and to the younger members, now both married, the deep sympathy of his colleagues is extended. He was looking forward to a happy period of retirement in a year or two, but this was not to be. He certainly was one well qualified to be included in those oft-quoted lines:

> Lo! some we loved, the loveliest and best
> That Time and Fate of all their Vintage prest,
> Have drunk their Cup a Round or two before
> And one by one crept silently to Rest.

J. C. R. writes: Forty-four years ago, at the Battle of Messines, I dressed a very young uncomplaining infantry officer, suffering from severe haemorrhage and extensive brachial-plexus injury. His only reaction was to suggest that many of the other wounded needed attention more than he did—so typical of the unselfishness and equanimity of Ivan McCaw. I will not write of his distinguished professional life but rather of the man, whom I knew intimately

and whose legion of admirers feel a deep sense of personal loss at his passing.

Ivan McCaw had a true genius for friendship and an infinite capacity for holding the esteem and affection of his friends. He was in the truest sense of the word—great gentle-man. In spite of his war disabilities he had a unique philosophy of life. He radiated good nature and kindness and never spoke a word of destructive criticism about people or colleagues. Ivan McCaw was a personality, a man of culture and of courage, and a good messmate. "He loved chivalrye, Trouthe and honour, fredom and curteisye."

HASHIM AL-WITRI, M.D., F.R.C.P.

Dr. Hashim Al-Witri, one of the leaders of the medical profession in Iraq and formerly professor of medicine and dean of the Faculty of Medicine in Bagdad, died on January 17. He was 71 years of age.

Hashim Al-Witri was born in Bagdad in 1898 during the Turkish occupation of Iraq, and it was natural for him to be educated at the Royal Military College, Istanbul. He graduated there in 1918, was soon commissioned as a captain in the medical services, and was posted back to his native city. In 1920 he was appointed physician to the New General Hospital, where he showed his aptitude as a clinician and a teacher. He came to London in 1928 and worked at the National Hospital, Queen Square, returning to Bagdad as professor of clinical medicine.

During the ensuing period he was dean of the Faculty of Medicine three times, first in 1938, in 1941–2, and again from 1946 to 1954. On his retirement in 1958 he was appointed emeritus professor of medicine. Although he had a gift for administration and played a prominent part in building up the College of Medicine, his main interest was in teaching medicine at the bedside. He founded the *Journal of the Faculty of Medicine of Iraq* in 1941 and remained its chief editor until his death. Among his contributions, many of which were in Arabic, were papers on clinical neurology, the history of medicine in Iraq, and first aid to the injured. He played a prominent part in the establishment of the Iraq Academy, of which he was vice-president. In 1950 he organized the Iraqi Medical Research Institute, which has made valuable contributions to the study of many local diseases. In recognition of his work he was, in 1948, elected a Fellow of the Royal College of Physicians of London. He was a member of the International Society of Internal Medicine, and, since 1948, representative of Iraq on that body. As an elder statesman and the dean of the Medical College during its formative years, he will be greatly missed.

W. R. M. D. writes: My first recollections of Professor Witri go back to my arrival in Bagdad in 1946. His kindliness and friendliness were at all times of great help to the British teachers. In his dealings with senior staff, technicians, and students he was always wise and understanding. He made a point of asking for their views and then of getting the best out of them. The position which the Medical Faculty now occupies owes much to his administrative ability, sound common-sense, and academic wisdom. He had a knowledge of the Iraqi medical student which few have possessed, and he was a good judge of them and of his fellow men. In spite of heavy responsibilities he accepted his local and international honours with modesty, insight, and a sense of humour.

G. A. MacDONALD, M.B., C.M.

Dr. G. A. MacDonald, who was formerly principal medical officer, Zanzibar, died at Gutach-Breisgau, Germany, on October 13, 1960. He was 91 years of age.

George Allardice MacDonald was born on the island of St. Vincent, British West Indies, on August 13, 1869, and received his early education in Bridgetown, Barbados, where he was already a keen gardener and botanist. Later he went to the University of Edinburgh and graduated M.B., C.M. in 1893. After holding several posts as house-physician and house-surgeon in Britain, he went to Zanzibar, where he was one of the first Europeans to practise modern medicine. Physician and surgeon to the Sultan and his court and to the European colony, he was also principal government medical officer and medical officer of health. In fact, he was personal physician to three Sultans, the reign of the last of whom extended until 1960, and he received numerous decorations from the court.

During the first world war Dr. MacDonald returned to the United Kingdom and worked at Dungavel, Shirlett, and Pinewood, being for a time medical superintendent of a sanatorium. In 1918 he returned to the British West Indies and in the next few years spent part of his time in Trinidad and part in London. He retired to Switzerland in 1939, first living at Blouay and later at Montreux, where he remained until his death.

Dr. MacDonald was a remarkable man who, despite failing eyesight, remained a phenomenally keen gardener until 1959. An elegant figure, a perfect listener, and a real *avant-quatorze* doctor, he had a well-developed sense of humour and would often tell intriguing stories of his experiences in Zanzibar. He maintained his optimistic outlook on life to the end of his days, and even in recent years was active enough to go on holiday to Madeira and to visit London. The local Swiss people among whom he lived recognized him immediately as *écossais*.

He is survived by his widow, a daughter, and four grandchildren.

K. J. ACTON DAVIS, M.Ch., F.R.C.S.

Mr. K. J. Acton Davis, formerly surgeon to the Queen Elizabeth Hospital for Children and to the Metropolitan Hospital, died at his home at Stockbridge, Hampshire, on February 10. He was 78 years of age.

Kenneth James Acton Davis was born on December 3, 1882. After reading classics at Cambridge he turned to the study of medicine, going on to St. Bartholomew's Hospital for his clinical training. There he won the Luther Holden research scholarship. Qualifying in 1911, he took the F.R.C.S. in 1913 and also proceeded to the degree of M.Ch. at Cambridge. After qualification he was house-surgeon and, later, chief assistant in the surgical out-patient department at his teaching hospital. During the first world war he served in the R.A.M.C. as a surgical specialist attached to the 11th General Hospital. On his return to London he entered consultant surgical practice and was elected to the staff of the East London Hospital for Children (now the Queen Elizabeth Hospital for Children), the Metropolitan Hospital, and St. Andrew's Hospital, Dollis Hill. He was also orthopaedic surgeon to the London County Council. Chairman of the City Division of the B.M.A. in 1935–6, he retired to Cornwall in 1938 and was high sheriff of that county in 1945. Thereafter he lived at Stockbridge in Hampshire.

Mr. Acton Davis is survived by his widow, one son, and three daughters.

An old friend and colleague writes: The death of Acton Davis has come as a real grief to his old friends and colleagues; though not unexpected, the event has saddened us all. He was, as regards his medical career, older than his actual contemporaries, since he had read classics at Cambridge and was a B.A. at the time when he, with most of those with whom, like myself, he was to be associated for the rest of his active life, entered on the training for his future profession. The same disparity of age applied, but did not last, when he came as a clinical student to Bart's, where he was later house-surgeon to Sir Anthony Bowlby, whose training formed him in his ideas and gave him an intensely practical outlook in surgery.

After serving in the first world war he returned to Bart's as one of the first group of the then new grade of chief assistant. He became surgeon to the Metropolitan Hospital

about the same time, and continued there until for family reasons he was obliged in 1938 to resign all his London appointments and retired to the country, where he spent the rest of his life.

Acton Davis was a big man, physically and in character. As a surgeon he attained wide experience and was always practical and human. Nothing was too much trouble for him when his patients needed him. He took great interest in the administration of the hospitals which he served, and again his outlook was always practical and of great value. His constant cheerfulness and his full enjoyment of life in all its forms, both in work and play, were always stimulating to his friends; and those of us who have known him well realize, though since retiring he was rarely in London, that we have lost a true and valued friend.

Medical Notes in Parliament

ROAD TRAFFIC BILL

The Government's new Road Traffic Bill* was published on Wednesday, March 22. It deals with unfitness to drive through drink or drugs; disqualification, endorsement, and penalties; speed limits; construction, use, and equipment of vehicles; driving instruction, minimum age, and test fees; highway powers; offences in Scotland; and various miscellaneous matters. There are also three schedules. The first lists offences for which disqualification is obligatory or discretional and amends other penalties. The second and third schedules repeal or amend other enactments.

Unfitness to Drive

Clause 1 re-defines the standard of unfitness to drive a motor vehicle through drink or drugs by providing that a person is to be taken as unfit if his "ability to drive properly is for the time being impaired." Clause 2 requires a court to "have regard to any evidence which may be given of the proportion or quantity of alcohol or of any drug which was contained in the blood or present in the body of the accused, as ascertained by analysis or measurement of a specimen of blood taken from him with his consent, or of water or breath provided by him, at any material time." A refusal, without reasonable cause, to provide a specimen for this purpose may be treated as supporting any evidence given by the prosecution, or as rebutting any evidence given by the defence, about the accused's condition.

The Clause goes on to explain that in such proceedings a certificate "purporting to be signed by an authorized analyst, and certifying the proportion of alcohol or any drug found in a specimen identified by the certificate and, in the case of a specimen not being a specimen of blood, the proportion of alcohol or of that drug in the blood which corresponds to the proportion found in the specimen" shall be evidence of the matters certified and of the qualification of the analyst. An "authorized analyst" is defined as a person possessing the qualifications prescribed by regulations made under Section 89 of the Food and Drugs Act, 1955, or Section 27 of the Food and Drugs (Scotland) Act, 1956, as qualifying persons for appointment as public analysts, "and any other person authorized by the Secretary of State to make analyses for the purposes of this section."

Compulsory Disqualification

Clause 3 makes new provision for disqualification from holding a driving licence on conviction of certain offences. In the absence of special reasons, the Court *must* disqualify for at least 12 months—or, in the case of an offence of driving while under the influence of drink or drugs committed within 10 years of a previous offence, for at least three years—on conviction of the following offences: manslaughter, causing death by dangerous driving, dangerous driving within three years of a previous similar conviction, "racing," driving while disqualified, and using a motor vehicle uninsured or unsecured against third-party risks. The Clause also provides for discretionary disqualification by Courts in respect of 16 other offences, which include being in charge of a motor vehicle while under the influence of drink or drugs, failure to comply with traffic directions, leaving a vehicle in a dangerous position, contravention of pedestrian-crossing regulations, failure to stop and give particulars after an accident, and parking without lights on a road. Maximum fines for various offences are also raised.

Some Other Provisions

Clause 9 gives power to the Minister of Transport to *direct* that a road shall become a 30 m.p.h. road. Clause 12, dealing with headlamps, requires them to comply "with such conditions as may be prescribed by regulation," and Clause 15 provides for the setting up of a register of driving instructors.

*The text is obtainable from Her Majesty's Stationery Office, price 2s. net.

BLOOD TESTS FOR PATERNITY

[FROM OUR PARLIAMENTARY CORRESPONDENT]

Lord AMULREE obtained a second reading for his Affiliation Proceedings (Blood Tests) Bill in the House of Lords on March 21, although Earl BATHURST, speaking for the Home Office, expressed some doubts about its provisions and even about its prospects of further progress. Two members of the House, Lady SUMMERSKILL and the Earl of LONGFORD, voted against it, but there were 72 (including three peeresses) in support of it.

Lord Amulree's Bill

Lord AMULREE recalled the earlier Bill introduced by Lord Merthyr in 1939 which got no further because of the war, and said the present Bill was the result of discussions which had been carried on for 10 to 12 years past, because of various changes in blood-grouping knowledge. The stage had now been reached when it could be said that, if they knew to what blood group the mother and child belonged, they could say that the father must belong to one of a certain number of blood groups. It could not be put much more definitely than that. If he did not belong to one of those groups he could not be the father of the child. He stated that in 1959 there were 4,996 applications for affiliation orders, of which 4,160 were granted. The number of those contested was not known. If the tests were applied it was estimated that 55 to 60% of men wrongly accused of paternity would be exonerated. He suggested that the best place for the tests to be carried out would be in the forensic medicine laboratories attached to the universities. At present there were four—Guy's Hospital, London Hospital, one in Sheffield, and one in Glasgow. About 200 tests a year were done under the voluntary system, and if the Bill were passed this might go up to about 1,000. Fees paid under the voluntary system were 12 guineas a test. The proposed Blood Tests Board would not in his opinion be an expensive set-up with a big secretariat and premises; he thought its expenses would not be more than travelling expenses. The Bill was a useful little Bill which would do justice to a few people who were suffering from an injustice.

Hard on Unmarried Mothers

Lady SUMMERSKILL criticized the Bill because some of its provisions were likely to bear hardly on the unmarried mother; because it was of very limited value—in two-thirds of the cases which would be subject to blood tests no inference could be valid—and because it did not weigh the scales of justice fairly between the man and the woman. The courts were empowered to dismiss the application of a mother who refused to submit to a test. The National Council for the Unmarried Mother and Her Child wanted some provision inserted to protect those who on religious

or other reasonable grounds refused to accept blood tests, and also desired that all certificates should be admitted as evidence and comment allowed on them, rather than have an air of mystery created about an inconclusive certificate. By accepting the Bill they might be putting into motion machinery which so far scientists could not say was perfect.

Greater Exactitude a Help to Courts

Lord TAYLOR took a contrary view. It was right that information about heredity, which had become available almost accidentally out of studies made for blood transfusion, should be made available to the law so that it could be more exact in what it sought to do. The validity of the tests was very high, the margin of error being of the order of one in 20,000—substantially less than when the previous Bill was introduced.

Lord MERTHYR, who sponsored the 1939 Bill, told the House that in his experience in no class of case coming before the courts—except poaching—was there a greater degree of perjury. Could it be wondered at if magistrates clutched at any straw to enable them to administer justice more easily? This Bill would be of some considerable assistance to the courts. It had been said that it would favour the man. So it would, but only if he had been wrongly charged with paternity, and in no other circumstances.

Government Doubts

The Earl of BATHURST began a cautionary tale by pointing out that Parliamentary time was running short for the "drastic" redrafting that might be necessary. The scientific principles underlying the Bill commanded general acceptance. In some cases the information would be of great assistance to the courts. What had to be considered was whether that justified the elaborate machinery that would have to be set up. Information in the Home Office was that blood tests were rarely carried out. They could not in any circumstances help the woman's case. The part they could play was still not widely known. It must be accepted that it was to some extent an infringement of individual liberties to enable an alleged father to oblige a woman to submit herself and her child to a test. The proposed Blood Tests Board might be a rather cumbersome edifice. The tests would have to be thorough and reliable, and might need staff and conditions different from those in the university laboratories that Lord Amulree had mentioned. In short, the Government were not happy about all the provisions in the Bill. They would wish to give it careful thought, and consult a number of persons and bodies interested if it went further.

QUESTIONS IN THE COMMONS

Executive Council's Decision Modified

The MINISTER OF HEALTH indicated in answer to questions on March 20 about his decision to modify the penalty imposed on an Essex doctor that he intended to publish the reasons why he had done so. But he refused on that occasion to be drawn into any discussion on the publication of the names of doctors who are "fined" by local executive councils.

Mr. M. LIPTON (Brixton, Lab.), who raised both issues, asked the Minister first why he had reduced the penalty of 50 guineas imposed by the Essex Executive Council on a doctor who failed to comply with his terms of service. Mr. ENOCH POWELL told him that before directing a withholding from the doctor's remuneration he considered not only the executive council's recommendation but also, as required by the regulations, the doctor's representations and the advice of the Medical Advisory Committee.

Mr. LIPTON: Is it not obvious that the Minister has ignored the decision of the local executive council? In this case the doctor refused to visit a 14-year-old boy dying of cancer and give him an injection to prevent unnecessary suffering. Does the Minister not think the time has come for him no longer to be a party to this covering up of guilty men, who should be named and punished like anyone else who does wrong? Mr. POWELL pointed out that Mr. Lipton's question did not raise the disclosure of names, on which practice had been uniform since the beginning of the Service. On the facts of the case he said: Of course I gave consideration to the recommendation of the executive council, and I am considering with the council the best method of publishing my reasons for the modification of the council's recommendation.

Mr. W. A. WILKINS (Bristol, South, Lab.): Will the Minister reconsider the practice of not publishing the name of the doctor concerned? There is no individual in any other walk of life who is protected by this privacy. There is a growing public feeling about this, and that the names should be disclosed. Mr. POWELL: The question of the name is a separate one, and it would be better if it were dealt with separately.

Mr. LIPTON asked when Mr. Powell intended to publish the further statement after consulting the executive council, and was told, "As soon as possible."

More Psychiatrists

Mr. KENNETH ROBINSON (St. Pancras, North, Lab.) asked the Minister what steps he was taking to stimulate the teaching of psychological medicine to medical students and to provide sufficient psychiatrists to man the expanding mental health services. Mr. POWELL said he had no powers with regard to the content of the medical curriculum. The number of senior registrar posts allocated to psychiatry and of consultants and senior hospital medical officers employed in this specialty had been increasing and continued to increase steadily. Mr. ROBINSON insisted that the rate of increase was nothing like adequate. Something like double the number of psychiatrists were needed. Did the Minister not appreciate that he would not get the necessary number unless he or somebody could do something about the content of medical education? Mr. POWELL said that the supply of consultants and others in this specialty had been increasing much faster than in other lines of medicine. The number of persons in training in the senior registrar grade indicated that the increase should continue. It was, however, the number that could be trained and the intake into training which ultimately determined the supply.

Mental Health Review Tribunals

Mr. KENNETH ROBINSON also asked how many applications had been made to mental health review tribunals in each region and from each of the special hospitals, respectively, since applications were first invited. Mr. POWELL gave him the following regional figures relating to valid applications up to March 16, 1961: Newcastle 0, Leeds 6, Sheffield (excluding Rampton Hospital) 2, East Anglia 1, North-west Metropolitan (excluding Broadmoor Hospital) 11, North-east Metropolitan 1, South-east Metropolitan 2, South-west Metropolitan 3, Oxford 1, South Western 3, Wales 6, Birmingham 10, Manchester 8, Liverpool (excluding Moss Side Hospital) 8, and Wessex 8. Special hospitals: Rampton 13, Moss Side 3, Broadmoor 0.

Casualty Services

Mr. RONALD RUSSELL (Wembley, South, Con.) was informed that the report of the Standing Medical Advisory Committee on the organization of casualty services was expected early next year. Mr. Russell suggested that it would be a good thing not to carry out the down-grading of certain hospitals, such as the Wembley hospital, for example, until this report was received. Mr. POWELL said he did not know the point Mr. Russell had in mind but he would look at it with him.

Sexual Aberration

Mr. POWELL stated in answer to Mr. LESLIE HALE (Oldham, West, Lab.) he was satisfied that the existing facilities were sufficient to enable a person suffering from serious sexual aberration to obtain voluntary treatment under the Health Service under conditions of secrecy.

Medico-Legal

THE RIGHT TO REFUSE MEDICAL EXAMINATION

[FROM OUR LEGAL CORRESPONDENT]

A usual procedure in personal injuries actions is for the injured plaintiff to submit himself to medical examination by his own doctors and then to examination by the defendant's doctors: the parties and their advisers then endeavour to agree a report to present to the Court. If a report is successfully agreed, the parties avoid the expense of calling opposing medical witnesses and cross-examining them.

But if the plaintiff refuses to submit himself to examination by a defendant's doctors, can he be compelled to do so? Is the rule any different from the case of a claim for injuries to the plaintiff's motor-car, which the plaintiff is certainly not bound to submit for examination by the defendant's mechanics?

There have been cases in recent years when the Master in Chambers in the High Court has ordered a personal injuries action to be stayed unless the plaintiff submitted himself to examination by the defendant's doctors. This indirect compulsion was disapproved by the Court of Appeal on March 16 (*The Times*, March 17; *Pickett v. Bristol Aeroplane Co. Ltd.*). In that action the plaintiff workman claimed that he had contracted dermatitis in the course of his employment. The plaintiff submitted to examination by two doctors for the defendant employers: one of those doctors subsequently died before trial, and the defendants requested the plaintiff to submit to examination by a distinguished dermatologist. The plaintiff objected to examination by this particular doctor. The Master refused the defendants' application that the action be stayed unless the plaintiff submitted to this examination. On appeal, the Court of Appeal held that the plaintiff was entitled to present his case in the way he wished. Refusal to be examined might be a matter for comment at the trial, but the plaintiff should certainly not be compelled to submit to examination by one particular doctor to whom he objected, and it was (to say the least) doubtful whether his action should be stayed even if he refused to submit to any examination by the defendants' doctors.

Vital Statistics

More Measles

In the early years of death-registration measles was a major cause of death. The peak year was 1896, when 17,618 deaths were registered. The number of deaths started to fall in 1916, and 1917 was the last year when the annual number of deaths exceeded 10,000. In 1958 only 49 deaths were registered from measles. Although the mortality has fallen dramatically the disease is as prevalent. The case fatality rate is now less than 2 in 10,000. Measles became notifiable on the outbreak of the second world war, and during the following ten years the notifications fluctuated between 300,000 and 400,000 a year. In 1951 the incidence was unusually high in the spring, and the annual number of cases rose to over 600,000. From this time measles has had a definite two-year periodicity; in the odd years the annual number of notifications have ranged from 532,000 to 691,000 and in the even years the range has been from 147,000 to 267,000. The largest weekly totals were those of the 6th and 7th weeks of 1953 and the 15th week of 1955, when over 32,000 cases were notified. These totals have been exceeded in the present epidemic: in the 8th, 9th, and 10th weeks of this year the notifications have numbered 34,863, 35,709, and 36,611 respectively.

Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

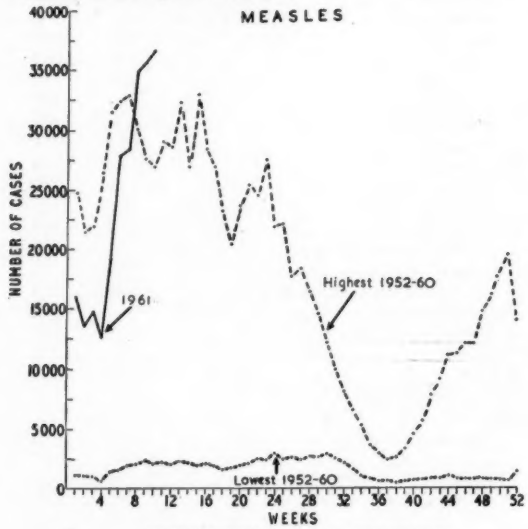
	Week Ending Mar. 4	Week Ending Mar. 11
Measles		
Durham	1,669	1,962
Sunderland C.B.	516	436
Essex	2,419	2,547
West Ham C.B.	260	214
Basildon U.D.	99	194
Chelmsford M.B.	92	176
Hornchurch U.D.	164	199
Ilford M.B.	139	212
Romford M.B.	207	192
Gloucestershire	260	380
Bristol C.B.	167	215
Hampshire	1,642	1,570
Southampton C.B.	558	296
Havant and Waterloo U.D.	133	281
Kent	1,735	1,827
Orpington U.D.	156	205
Lancashire	2,369	2,223
Manchester C.B.	313	300
Lincolnshire	502	799
London	3,403	2,986
Lambeth	279	213
Lewisham	372	272
Wandsworth	402	341
Woolwich	203	220
Middlesex	2,373	1,946
Harrow M.B.	197	226
Willesden M.B.	276	221
Northamptonshire	93	258
Northampton C.B.	53	182
Northumberland	583	568
Newcastle upon Tyne C.B.	260	224
Nottinghamshire	742	691
Nottingham C.B.	233	265
Staffordshire	1,088	1,442
Surrey	1,217	1,214
Croydon C.B.	154	215
Warwickshire	2,802	2,749
Birmingham C.B.	1,318	1,364
Coventry C.B.	701	577
Solihull M.B.	258	249
Meriden R.D.	140	200
Wiltshire	345	402
Swindon M.B.	221	280
Yorkshire East Riding	813	767
Kingston upon Hull C.B.	573	573
Yorkshire West Riding	2,147	2,448
Leeds C.B.	254	255
Sheffield C.B.	333	375
Glamorganshire	1,047	1,110
Cardiff C.B.	376	410
Dysentery		
Devonshire	19	57
Exeter C.B.	16	45
Durham	9	39
Darlington R.D.	0	20
Essex	69	57
Dunmow R.D.	9	16
Herefordshire	28	17
Hereford R.D.	19	15
Warwickshire	13	48
Birmingham C.B.	7	36
Yorkshire West Riding	226	210
Bradford C.B.	17	38
Leeds C.B.	72	57
York C.B.	18	52
Diphtheria		
Warwickshire	3	4
Birmingham C.B.	3	4
Glasgow	3	4

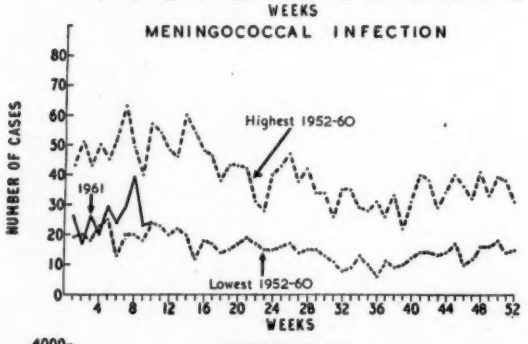
Population of Pakistan

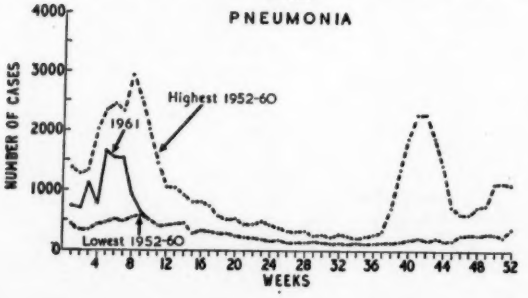
The provisional results of the 1961 census held in Pakistan show an increase of 23.7% over the population in 1951. The estimated population now is 93.8 million—49.2 million men and 44.5 million women. About 50 million live in East Pakistan, 40 million in West Pakistan, and over 2 million live in the Federal territory of Karachi. It was estimated that 15.3% of the total population were literate. Announcing these results, the Minister for Home Affairs said that the increase in population was alarming, and that in the next 40 years the population of the country would be doubled.—*Pakistan News*, March 15, 1961.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1952–60 are shown thus ------, the figures for 1961 thus ———. Except for the curves showing notifications in 1961, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.







INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **March 11** (No. 10) and corresponding week 1960.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1961					1960				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	6	1	4	0	3	3	1	1	0	1
Dysentery	729	52	113	11	4	1,844	196	192	27	9
Encephalitis, acute	1	0		0		2	0	0	0	
Enteric fever:										
Typhoid	0	0		0	} 1	{ 1	0	0	0	0
Paratyphoid	2	0		0		{ 10	0	1	0	1
Food-poisoning	94	12	19	1		193	26	3	5	
Infective enteritis or diarrhoea under 2 years				9	23				12	14
Measles*	36,611	2986	676	580	563	2,141	90	83	5	36
Meningococcal infection	24	2	12	1	1	25	4	6	0	2
Ophthalmia neonatorum	25	2	3	0		29	0	3	0	
Pneumonia†	512	33	234	31	14	501	29	203	14	8
Poliomyelitis, acute:										
Paralytic	3	0	0	} 0	1	{ 6	0	0	} 0	
Non-paralytic	2	0	0			{ 3	0	1		
Puerperal fever§	180	30	11	1		203	28	5	0	
Scarlet fever	514	39	36	34	14	1,077	34	59	16	24
Tuberculosis:										
Respiratory	375	63	60	7		455	38	62	6	
Non-respiratory	62	3	12	2		70	6	13	8	
Whooping-cough	955	25	68	8	89	782	49	171	10	30

DEATHS	1961					1960				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		0	0		0	
Encephalitis, acute	1	0			0					0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	9	0	0	0	1	12	0	1	0	0
Influenza	197	7	14	2	4	35	1	1	1	0
Measles		0	0	0	0	0	0	0	0	0
Meningococcal infection		0	1				0	1		
Pneumonia	808	58	37	23	7	708	52	21	13	12
Poliomyelitis, acute	0	0		0	0	1	1		0	0
Scarlet fever	0	0	0	0	0	0	0	0	0	0
Tuberculosis:										
Respiratory	} 68	{ 2	} 6	1	5	} 89	{ 3	9	0	4
Non-respiratory		{ 1		0	0		{ 3	0	0	0
Whooping-cough	0	0	0	0	0	1	0	0	0	0
Deaths 0–1 year	314	28	35	7	15	369	33	27	6	10
Deaths (excluding stillbirths)	11,470	891	701	151	211	11,119	880	619	136	215
LIVE BIRTHS	16,383	1386	1098	280	417	15,574	1323	992	271	337
STILLBIRTHS	318	24	18			325	23	18		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Wolfson School of Nursing, Westminster Hospital

Westminster Hospital's new Wolfson School of Nursing in Vincent Square was opened by QUEEN ELIZABETH THE QUEEN MOTHER on March 23. It has been financed by the first major grant the Wolfson Foundation made—one of £250,000. The school, which provides training both for the Children's Register of Nurses and for the General

Wolfson School of Nursing.

Register, can take 200 trainees at any one time, in courses of 27 weeks divided over a period of three years. The building consists of a partial basement, a ground floor, and four upper floors with the roof designed as a recreation space and garden. Apart from assembly room, lecture rooms, and demonstration wards of every kind, and with every kind of equipment, there is on the third floor a science room, a practical anatomy classroom, and a museum. On the fourth floor there is, in addition to the students' main common-room, the Edwina Mountbatten Library with shelf space for 7,000 books. Books on non-medical subjects have been bought with an additional personal gift made by Mr. and Mrs. ISAAC WOLFSON. Between 1,300 and 1,500 students apply for training each year to Westminster Hospital and Westminster Children's Hospital, and of this number 180 are selected. (Architects: T. P. Bennett and Son. Photograph by courtesy of the *Nursing Times*.)

McIndoe Memorial Research Unit

The McIndoe Memorial Research Unit was opened on March 22 at Queen Victoria Hospital, East Grinstead, by the Minister of Health, Mr. ENOCH POWELL. A wall plaque in the unit shows the head of Sir Archibald McIndoe in relief and states that the building was presented by Elaine and Neville Blond to commemorate the pioneer surgery of Sir Archibald. Research will be carried out there on wound healing and tissue transplantation. Mr. NEVILLE BLOND has contributed £40,000 towards building and equipping the department, which has grown considerably in scope since it was first planned as the Blond Laboratories in 1958. Sir MILES CLIFFORD, chairman of the Leverhulme Trust, has provided a grant of £4,000 a year for seven years to finance a research Fellow—at present Dr. A. D. BARNES—and technicians. Messrs. Johnson and Johnson (Great Britain) Ltd. have given £3,000 a year for seven years to be used in the same way. The building contains six laboratories, a technical workshop, animal rooms, Fellows' and administrative offices, a refrigerated cold-room, store-rooms, and a photographic dark-room.

Royal Flying Doctor Service of Australia

The Royal Flying Doctor Service of Australia, which was recently in need of recruits (*B.M.J.*, March 25, p. 897) is now up to its full strength.

Carlsberg–Wellcome Travelling Research Fellowships

Applications—to be submitted before April 30—are invited for the Carlsberg–Wellcome Travelling Research Fellowships, 1961–2, the object of which is to encourage co-operation, on an exchange basis, between Danish and British research workers in any branch of the natural sciences which has a bearing upon human and animal medicine. Details may be obtained from the Assistant Scientific Secretary of the Wellcome Trust, 52 Queen Anne Street, London W.1.

One Fellowship annually is awarded to a candidate from the United Kingdom for a year's work in Denmark and one annually to a Danish candidate for a year's work in the United Kingdom. The stipend may range from £900 to £1,300 per annum (or the equivalent sums in Danish kroner), travelling and some incidental expenses being provided in addition. The tenure of the awards will start in September, 1961.

James IV Surgical Association

A James IV Surgical Association commemorating that Scottish prince's position in the history of surgery—he established the Royal College of Surgeons of Edinburgh in the first decade of the sixteenth century—was founded in informal circumstances in 1957 at the meeting of the American College of Surgeons in Atlantic City. Since that time the James IV Surgical Association has been incorporated as an American company, and the first King James IV Travelling Fellowship has been established by an American industrialist, Mr. DAVID MARX. It is hoped that eventually about a dozen of these annual Fellowships, enabling working surgeons to travel overseas for a period of six weeks, will be established. The first James IV Travelling Professor this year will be Mr. J. J. M. BROWN, lecturer in paediatric surgery, Edinburgh University, who will visit the U.S.A. and Canada. An anonymous donor has made a second Fellowship possible for later in the year.

Medical Journals for Overseas

The British Supporting Group of the World Medical Association started a scheme in January, 1960, for sending copies of medical journals to colleagues overseas (see annotation, *B.M.J.*, January 23, 1960, p. 261). A progress report on a pilot scheme for sending journals to India says that about 1,450 used copies of the *British Medical Journal*, the *Lancet*, and the *Practitioner* are being sent to 150 honorary secretaries of divisions of the Indian Medical Association for circulation to their members. Many appreciative letters have been received from India, and those who would like to pass their journals on in this way should write for details of the scheme to the Honorary Secretary, British Supporting Group of the World Medical Association, B.M.A. House, Tavistock Square, London W.C.1.

Rogers Prize, London University

Applications for the Rogers Prize (£100) for an essay or dissertation on "The Causes and Results of Arterial Thrombosis in Man," open to all those on the medical register of the United Kingdom, must be submitted to the Secretary to the Scholarships Committee, University of London, Senate House, London W.C.1 (from whom details can be obtained) by April 30, 1962.

"Journal of Atherosclerosis Research"

The new bi-monthly *Journal of Atherosclerosis Research* is to be an international journal of fundamental research into atherosclerosis and related subjects. The editorial secretary is Dr. F. P. WOODFORD (36 Witte Singel, Leyden, the Netherlands), and Dr. G. S. BOYD (department of biochemistry, Edinburgh University) and Dr. J. C. POOLE (Sir

William Dunn School of Pathology, Oxford University) are members of the international editorial board. The journal is published in English and summaries are provided in French and German. The subscription is £6 5s. ($17.50; Dfl. 66.50) a year, and inquiries should be addressed to the publishers, Elsevier Publishing Company, 110–112 Spuistraat, Amsterdam-C, the Netherlands.

Change of Name

The Society of American Bacteriologists, which was founded in 1899, has changed its name to the American Society for Microbiology.

In Brief

W.H.O. reports that the total number of doctors in Albania has increased from 102 in 1958 to 444 in 1960, and that of paramedical workers from 136 in 1958 to 2,927 in 1960. About 90 doctors a year graduate from the Tirana University Faculty of Medicine.

A special five-year course to train doctors from developing countries is to be started by the Medical School of the Hebrew University in Jerusalem.

A tender figure of £1,955,131 has been accepted for the main stage of the new hospital for West Cumberland at Heasingham, near Whitehaven. Work on this stage, which will provide 350 beds, is expected to start in April and end three and a half years later.

People in the News

Mr. MICHAEL WARD, a London surgeon and a member of the 1953 Everest expedition, is among a group of climbers who have climbed the 22,300-ft. peak of Ama Dablam, near Everest. In 1959 two climbers from a British expedition were lost in an unsuccessful attempt to scale the mountain, which is considered to be one of the most difficult in the Himalayas. Mr. Ward, who is with a party of scientists undertaking physiological experiments with Sir EDMUND HILLARY'S Himalayan expedition, became interested in climbing while at Marlborough. He climbed in the Scottish Highlands, the Lake District, Wales, and in the Alps, and gained his first experience of Himalayan climbing in the 1951 reconnaissance expedition. He was educated at Marlborough and Cambridge University, and qualified from the London Hospital in 1949, gaining his F.R.C.S. in 1955. He is a Hunterian professor of the Royal College of Surgeons of England. Photograph by courtesy of the Royal Geographical Society and Alpine Club of Great Britain.

Lord COHEN OF BIRKENHEAD has been elected as President of the National Society for Clean Air, for the usual two-year term of office. He succeeds Sir HUGH BEAVER, chairman of the Government committee whose report in 1954 led to the passing of the Clean Air Act.

Professor T. ANDERSON, University of Glasgow, is undertaking a two-month lecture tour of Canada at the invitation of the Canadian Thoracic Society.

Dr. J. BIERER, medical director, Marlborough Day Hospital, will be lecturing at many universities, hospitals, and societies throughout the U.S.A. in April and June.

COMING EVENTS

Anglo-American Medical Society.—Meeting, "The Artificial Kidney and Its Place in Medicine To-day," April 7, R.A.F. Hospital, Ely. Speaker: Group Captain R. C. JACKSON. Buffet and bar from 7.30 p.m.; meeting 8.30 p.m. Admission by ticket only.

Symposium on Sterilization.—Organized by Department of Pharmaceutical Sciences of Pharmaceutical Society of Great Britain, with Smith and Nephew Research Ltd., April 11–13, Assembly Hall, School of Pharmacy, University of London, Brunswick Square, London W.C.1. Details from Society at 17 Bloomsbury Square, London W.C.1.

Lumleian Lectures.—Dr. L. J. WITTS, "Some Aspects of the Pathology of Anaemia," April 11 and 13. See advertisement p. 42.

Emily Blake Memorial Lecture.—Professor T. N. A. JEFFCOATE, "Pre-malignant Lesions of the Vulva," April 12, 5.30 p.m., Royal Victoria Infirmary, Newcastle upon Tyne.

Family Planning Association.—Training service for medical practitioners. See advertisement p. 42.

British Orthopaedic Association.—Spring meeting, April 13–15, University Union Debating Hall, Oxford Road, Manchester. Subjects include injuries to the neck; bone metabolism; fractures. Details from B.O.A., 47 Lincoln's Inn Fields, London W.C.2.

Nutrition Society (Scottish Group).—Symposium, "The Relative Values of Animal and Vegetable Fats in Nutrition," April 22, 1.30 p.m., Physiology Lecture Theatre, Queen's College, Dundee. Chairman: Professor A. C. FRAZER (department of medical biochemistry and pharmacology, Birmingham University). Details from Dr. J. DAVIDSON, Rowett Research Institute, Bucksburn, Aberdeen.

Lister Oration.—Professor WILDER G. PENFIELD, O.M., "The Brain's Record of Experience," April 27, 4 p.m., Royal College of Surgeons of England, Lincoln's Inn Fields, London W.C.2.

London Association of Royal College of Surgeons in Ireland.—Annual dinner and dance, April 27, Rembrandt Hotel, London S.W.1. Details from Honorary Secretary, 56 Glenister Park Road, London S.W.16.

Naval Medical Compassionate Fund.—A meeting of the subscribers to elect six directors, April 28, 2.30 p.m., Medical Department of Navy, Queen Anne's Mansions, St. James's Park, London S.W.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Tuesday, April 4

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. H. C. Grant: Chronic Meningitis.

Wednesday, April 5

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., Dr. I. Friedmann, Dr. D. A. Osborn, and Dr. A. L. Jeanes: clinical pathological conference.

Thursday, April 6

NORTH-WESTERN THORACIC SOCIETY.—At Victoria Hospital, Blackpool, 3.30 p.m., clinical meeting.

Friday, April 7

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—(1) 3.30 p.m., clinical discussion for general practitioners. Mr. G. H. Howells: Dysphagia. (2) 5.30 p.m., open lecture and demonstration for trainees in the specialty. Mr. Anthony Radcliffe: Surgery or Radiotherapy for Cancer of the Throat.

SOCIETY OF MEDICAL OFFICERS OF HEALTH: SERVICES GROUP.—At Committee Room C, B.M.A. House, Tavistock Square, London W.C., 5.30 p.m., Squadron Leader T. G. Dobie, R.A.F.: Physiological Tests and Training of Future Pilots.

WHIPPS CROSS HOSPITAL MEDICAL SOCIETY.—8.30 p.m., Flight Lieutenant John Billingham: Space Medicine.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Thomas.—On March 17, 1961, at St. David's Hospital, Bangor, to Aisla, wife of Dr. Gareth Hughes-Thomas, of Iet Wen, Morfa Nefyn, Pwllheli, Caerns, a daughter—Alison.

DEATHS

Cresdee.—On March 16, 1961, William Charles Cresdee, M.R.C.S., L.R.C.P.

McCann.—On March 19, 1961, John Joseph McCann, M.B., B.S., of Scarlets, New Wokingham Road, Crowthorne, Berks.

Milne.—On March 14, 1961, William Alexander Milne, M.B., Ch.B., D.P.H., of 7 The Green, St. Leonards-on-Sea, Sussex, aged 82.

Nelson.—On March 10, 1961, John Joseph Harper Nelson, C.I.E., O.B.E., *M.C.*, M.D., F.R.C.S.Ed., Colonel I.M.S., retired.

Rees.—On March 22, 1961, at Cardiff Royal Infirmary, Llewellyn Rees, M.R.C.S., L.R.C.P., of 77 Cyncoed Road, Cardiff, aged 55.

Robertson.—On March 14, 1961, John Douglas Robertson, M.D., F.R.C.P., D.P.H., F.R.S.Ed.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Sensitivity to Barbiturates

Q.—*Are there any harmful effects from the long-term administration of a short-acting barbiturate—that is, quinalbarbitone sodium—in divided doses up to 600 mg. a day? Is addiction to such a short-acting barbiturate less harmful than alcoholic addiction?*

A.—Individual sensitivity to barbiturates varies considerably, and doses which are well tolerated by some patients may be undesirable in others. On 600 mg. of quinalbarbitone sodium daily, some motor incoordination and inadequate social adjustment are likely to occur, with the risk of subsequent increase in the patient's difficulties. This dose is on the borderline of what is liable to cause addiction, and tremor, excitability, and convulsions are to be expected on withdrawal. There is little to choose between the evils of addiction to either barbiturates or alcohol. A valuable account of chronic barbiturate intoxication is given by Isbell *et al.*[1]

REFERENCE

1 Isbell, H., Altschul, S., Kornetsky, C. H., Eisenman, A. J., Flanary, H. G., and Fraser, H. F., *Arch. Neurol. Psychiat. (Chicago)*, 1950, **64**, 1.

Medicinal Value of Garlic

Q.—*It is said that garlic is an intestinal antiseptic and that it destroys round- and thread-worms. It is also said that garlic lowers blood-pressure. Is there any evidence to support these claims?*

A.—Preparations made from the fresh bulb of *Allium sativum* (garlic) have been shown to have expectorant, antiseptic, diaphoretic, and diuretic properties. They have not been generally used therapeutically in this country because there are better substances available and because the rather overpowering odour of garlic is not as socially acceptable as it is in some Continental countries. Suppositories containing an extract of garlic have been successfully used for the treatment of threadworms in children, but for this purpose piperazine is a better and more reliable preparation. Recently an antibiotic substance with considerable antibacterial activity, allicin, has been obtained from garlic. This is produced by the interaction of an enzyme on a substrate; both of these are present in the garlic bulb, but they interact only when the bulb is crushed. It has been shown that allicin inhibits sulphydryl enzymes and that it has some effect as an antimitotic agent.[1,2] Although there are reports in the Continental literature that garlic preparations have some effect in lowering blood-pressure in hypertension, this work has not been confirmed either in this country or in America.

REFERENCES

1 Wills, E. D., *Biochem. J.*, 1956, **63**, 514.
2 Weisberger, A. S., and Pensky, J., *Science*, 1957, **126**, 1112.

Prophylaxis Against Respiratory Infections

Q.—*Would continuous antibiotic or sulphonamide treatment be advisable and helpful as a prophylactic against upper respiratory infections in a child aged 4 who has had persistent coryza and otitis media since starting school three months ago? If so, what antibiotic or long-acting sulphonamide is safe and effective? The tonsils appear healthy; there is no sign of adenoids; and ear, nose, and throat swabs grew only mixed pathogens.*

A.—Firstly, none of the antibiotics on the market are effective against either the common cold or any other virus. Secondly, many of the unpleasant and prolonged consequences of colds are due to bacterial infection. The latter may be prevented or cured by treatment with the appropriate drug, whether sulphonamide, penicillin, or broad-spectrum antibiotic, in adequate dosage. On the other hand, established upper respiratory, sinus, or tonsillar infections can be very resistant to antibiotic treatment.

There has been a certain amount of work to suggest that prophylactic sulphonamide and penicillin treatment may reduce the apparent frequency and severity of upper respiratory infections. In one trial[1] the patients were given sulphadimidine 0.5 g. daily with good results. The efficiency of prolonged daily treatment with small doses of antibacterial drugs must, however, be viewed with a certain amount of scepticism. Daily treatment with adequate therapeutic doses large enough to produce a bactericidal blood-level is likely to be more effective, but, of course, is expensive. Prolonged treatment with chloramphenicol and, to a less extent, with sulphonamides could have a harmful effect on blood formation. Bacterial resistance is almost certain to develop in the course of time. It may therefore be asked why daily prophylactic treatment with penicillin for several years is advocated after an attack of rheumatic fever. The answer to this is that the dose of penicillin given is fairly large; a specific organism, the haemolytic streptococcus, is the object of attack; and this organism does not develop resistance to penicillin. Furthermore, the importance of preventing further attacks outweighs lesser disadvantages.

To sum up, the value of daily prophylactic antibacterial treatment in the prevention of upper respiratory infections has not been well established. The disadvantages make its adaptation on a large scale inadvisable. It may be worth trying out in specific instances. Penicillin V 65 mg. daily would probably be the best and safest drug to use in the case of a 4-year-old child for the rest of the winter. The evidence that the tonsils and adenoids are healthy in the face of the persistent cough and otitis media would seem a contradiction of the usual findings.

REFERENCE

1 Burke, J. B., *Brit. med. J.*, 1956, **1**, 538.

Intrauterine Contraceptives

Q.—*I have recently been asked about a new plastic intrauterine contraceptive appliance. Could you tell me about its general advisability, efficacy, and method of insertion? Has it overcome the danger of carcinogenesis?*

A.—Despite a spirited defence of them by Oppenheimer,[1] intracervical and intrauterine contraceptive appliances are in general disfavour. This is because they are considered harmful and inefficient—the former because they may cause discharge, menorrhagia, and dysmenorrhoea, as well as infection (rather than cancer), and the latter because the appliance may be expelled without the patient's knowledge and because the uterus may on occasion harbour both pregnancy and device. The writer has no experience of such appliances made of plastic, but, since this is generally inert and non-irritant, it seems logical to believe that a plastic device would be less dangerous and less efficient. Strictly speaking, intrauterine appliances are not contraceptive devices but abortifacients, inasmuch as they promote an endometrial irritation which interferes with the normal implantation of the fertilized ovum, as well as stimulating uterine contractions, as a foreign body.

REFERENCE

1 Oppenheimer, W., *Amer. J. Obstet. Gynec.*, 1959, **78**, 446.

Diagnosing Mumps

Q.—*Can a bilateral parotitis in which there was a ten-day interval between the incidence of swelling on the two sides be accounted for by mumps? The parotitis was associated with a concurrent attack of measles in a child aged 6.*

A.—An interval of five days between the swellings of the two sides of the face in mumps has been reported by several authors, but an interval of ten days makes the

diagnosis of mumps unlikely, though not impossible. Measles is not uncommonly associated with cervical adenitis, presumably due to secondary infection, and swellings due to this may have occurred in this case and led to difficulty in diagnosis. Mumps can be a disease very difficult to diagnose clinically, and a retrospective diagnosis, without serological aid, is impossible.

Cleaning Syringes

Q.—*How is it possible to prevent a deposit from forming gradually inside the barrel of syringes, to the extent of preventing insertion of the piston, and to clean it off after it forms? We rinse and clean our syringes after use and before sterilizing in an electric sterilizer. The water is hard in this district.*

A.—Does the reference to hard water mean that the "electric sterilizer" is an electrically heated boiler in which tap water is used? If so, the remedy is to use distilled water: this is cheap enough in bulk and consumption should be small. If dry sterilization in an electric oven is meant, then again final thorough rinsing in distilled water before sterilization is important. Other precautions are immediate rinsing after use, especially such a use as the withdrawal of blood, and treatment with a suitable detergent before final rinsing and resterilization.

NOTES AND COMMENTS

Phenothiazine Derivatives.—Dr. S. G. BAYLISS (Welwyn, Herts.) writes: The question about the meaning of words used in current psychiatric jargon ("Any Questions?" February 25, p. 605) raises more important issues than that of terminology. The exact mode of action of many of the drugs in use to-day is still obscure, but certain pharmacological actions have been demonstrated and should be more widely known. During recent months I have been alarmed to meet several psychiatrists who have had little knowledge of the pharmacology of the drugs they used and were unaware of the possible dangers. It is hardly surprising that unexpected and sometimes dangerous side-effects occur when two or more potent psychotropic drugs are used in combination without regard to possible interaction. For example, monoamine-oxidase inhibitors block the action of the enzyme responsible for the breakdown of 5-hydroxytryptamine (serotonin) and related amines. Reserpine can be shown to release stored 5-hydroxytryptamine from its binding sites. If reserpine is given during or immediately following a course of treatment with a monoamine-oxidase inhibitor, large quantities of 5-hydroxytryptamine are released but not destroyed in the normal way because the enzyme is inhibited.[1] [2] This produces additional stimulation and will precipitate excitement or even mania. Reserpine should not be used as a "tranquillizer" in combination with this type of anti-depressant drug.[3] Such occurrences are fortunately rare but are due to a lack of detailed knowledge of the drugs in use. As your answer rightly points out, some terms used to-day are of little value but will inevitably remain with us for some time yet. Meanwhile some knowledge of pharmacological and biochemical actions of these drugs will minimize confusion.

REFERENCES

1 Besendorf, H., and Pletscher, A., *Helv. physiol. pharmacol. Acta*, 1956, **14**, 383.
2 Shore, P. A., and Brodie, B. B., *Proc. Soc. exp. Biol. (N.Y.)*, 1957, **94**, 433.
3 Brune, G. G., and Himwich, H. E., *Science*, 1961, **133**, 190.

OUR EXPERT replies: I would agree entirely with Dr. Bayliss that the issues raised by the introduction of numerous new drugs into psychiatric and general medical practice within recent years extend well beyond the question of terminology and that some knowledge of the pharmacological actions of the drugs and of the biochemical effects which they are known to bring about in the nervous system is essential before one starts to use any of these potent substances. Questions of pharmacology and the use of these drugs either singly or in combination were, however, outside the scope of the original question, which was concerned only with the classification of the numerous terms which have been adopted to describe these new preparations.

Oestrogens in the Climacteric.—Mr. E. SCHLEYER-SAUNDERS (London W.1) writes: In reply to this question ("Any Questions?" February 18, p. 521) the expert expresses the still commonly held view that continuous oestrogen therapy is inadvisable for two reasons: (1) it may lead to prolonged uterine bleeding; and (2) it carries a "*theoretical*" (my italics) possibility of carcinogenesis. I must admit that I held the same view until 16 years ago, when I started treating menopausal women with implants of oestradiol and testosterone according to the condition of the uterus and the vaginal cytological test (Papanicolaou or P.A.P. test). This test shows the degree of oestrogen deficiency and the presence of abnormal epithelial cells indicating the possibility of a malignant condition. In a recent paper[1] I published the results of 500 menopausal women treated with implants. Before using the cytological test and implanting oestrogens heavy uterine bleeding occurred in some cases, but among the last 400 patients treated with the combination of oestradiol and testosterone no bleeding occurred. Occasional spotting is of no importance if the P.A.P. test is negative. As to the possibility of the carcinogenic effect of oestrogens, this is one of many other cancer theories, and is based on experiments in the lower animals, but, so far, clinical observations have failed to substantiate this theory. On the basis of a large amount of clinical evidence in the literature, quoted in my paper, and my own experience, I am led to the conclusion that there is no convincing evidence that oestrogen has ever produced cancer in human beings. Oestrogen is, however, a growth-promoting hormone, and if a symptomless cancer is stimulated by oestrogen the symptoms will be shown earlier; this promoting action can be a blessing in disguise, as women will be induced to seek medical advice at an early stage of the illness. The advantage of implants is that resorption is very slow and withdrawal is also gradual, and the patient is not continuously being reminded of her condition by having to take tablets or receive injections at regular intervals. Implants are given not only to relieve climacteric symptoms but also to slow down the progressive process of ageing. Pre-operative implants in senile women who have to undergo operation for genital prolapse restore the vaginal mucosa to such a favourable condition as to make dissection easier and recovery speedier.

REFERENCE

1 Schleyer-Saunders, E., *Med. Press*, 1960, **244**, 337.

OUR EXPERT replies: Mr. Schleyer-Saunders may well be right in regarding the case against oestrogens, no matter how administered, being carcinogenic agents in the human as unproven. However, in the light of experimental evidence of a difference between continuous and discontinuous administration in their tumour-inducing effects in animals, most authorities agree that continuous administration of oestrogen is, in general, best avoided. The slow resorption of implants, though advantageous from one point of view, is a distinct drawback from another—namely, the loss of control of therapy, other than by the inconvenient expedient of removal of the implant, should oestrogen therapy no longer be desired. The fact is, of course, that the climacteric syndrome is usually a fluctuating condition, and for this reason oral administration has the obvious advantage of flexibility permitting more nicely adjusted control than is possible with implants.

Corrections.—We regret there were two mistakes in the obituary of Dr. James Reid (March 4, p. 678). Dr. Reid was survived by a widow and three sons and a daughter; and the second appreciation should have been introduced with the initials R. A. J.

"Naseptin" cream (I.C.I.) contains neomycin and "hibitane" hydrochloride and not neomycin and hexachlorophane, as stated in the answer to a question on chronic furunculosis ("Any Questions?" March 18, p. 842).

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